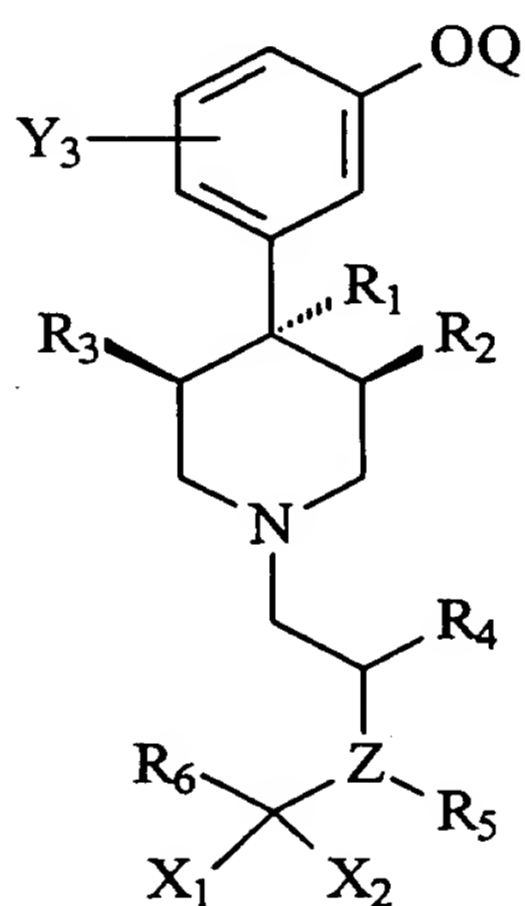


IN THE CLAIMS

Please amend the claims as follows:

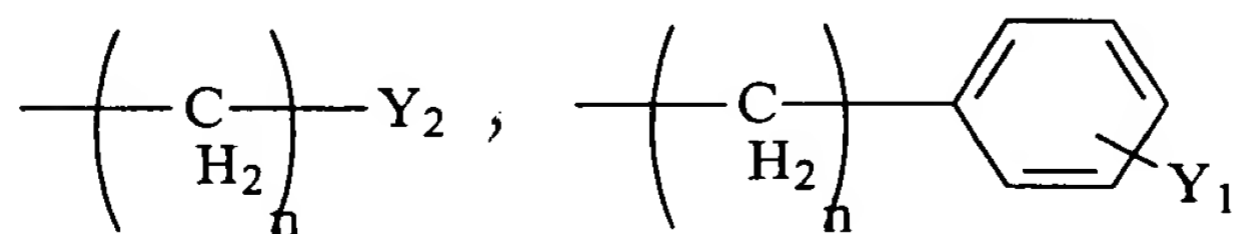
--1. (Currently Amended) A method of binding a kappa opioid receptor in a subject in need thereof, comprising:

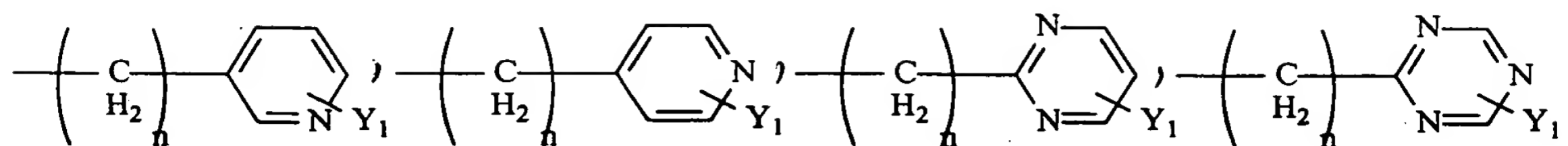
administering to said subject a composition comprising a kappa opioid receptor antagonist and a physiologically acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula (I):



wherein Q is H or COC₁₋₈ alkyl;

R₁ is C₁₋₈ alkyl, or one of the following structures:





Y₁ is H, OH, Br, Cl, F, CN, CF₃, NO₂, N₃, OR₈, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂,
 B8 NHCO₂R₁₂, CONR₁₃R₁₄, or CH₂(CH₂)_nY₂;

Y₂ is H, CF₃, CO₂R₉, C₁₋₆alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, CH₂OH,
 CH₂OR₈, or COCH₂R₉;

Y₃ is H, OH, Br, Cl, F, CN, CF₃, NO₂, N₃, OR₈, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂,
 NHCO₂R₁₂, CONR₁₃R₁₄, or CH₂(CH₂)_nY₂;

R₂ is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl or CH₂aryl substituted by one or more
 groups Y₁;

R₃ is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl or CH₂aryl substituted by one or more
 groups Y₁;

wherein R₂ and R₃ may be bonded together to form a C₂₋₈ alkyl group;

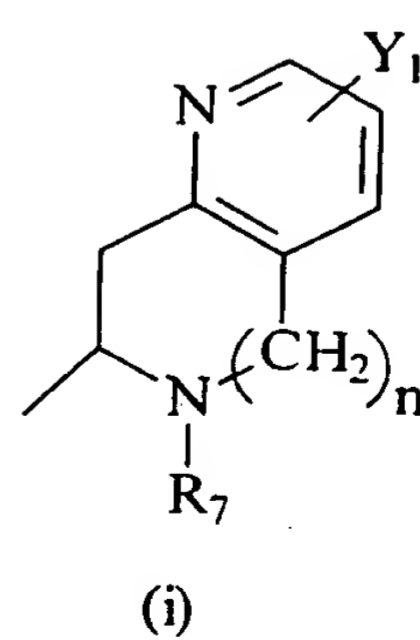
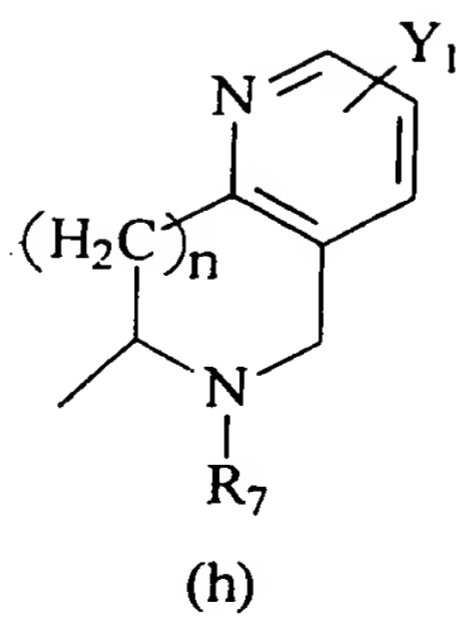
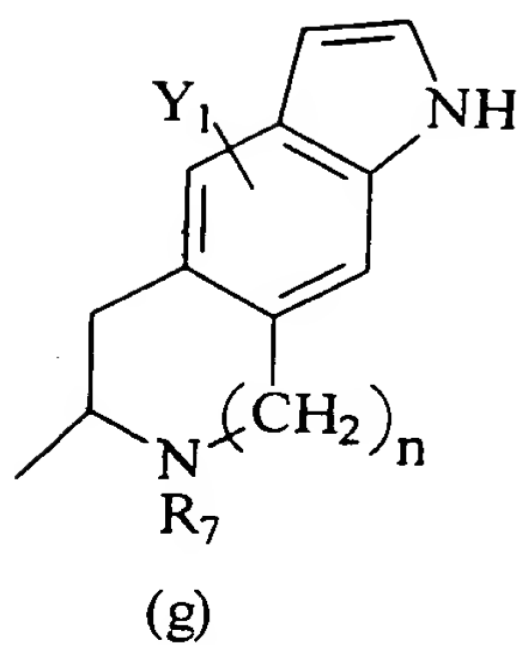
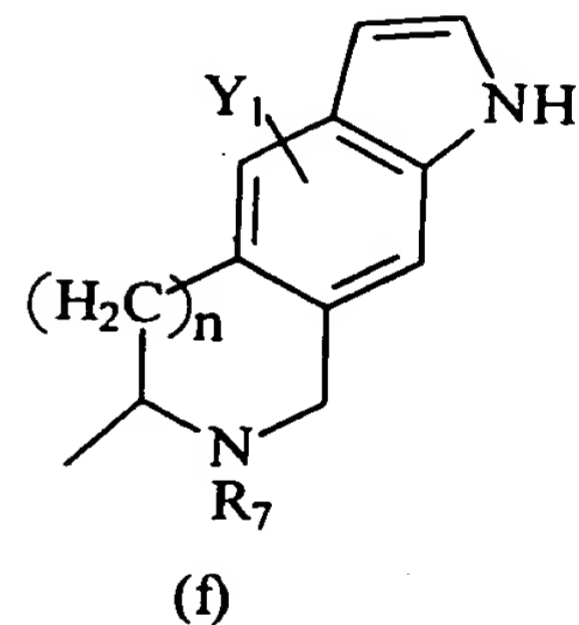
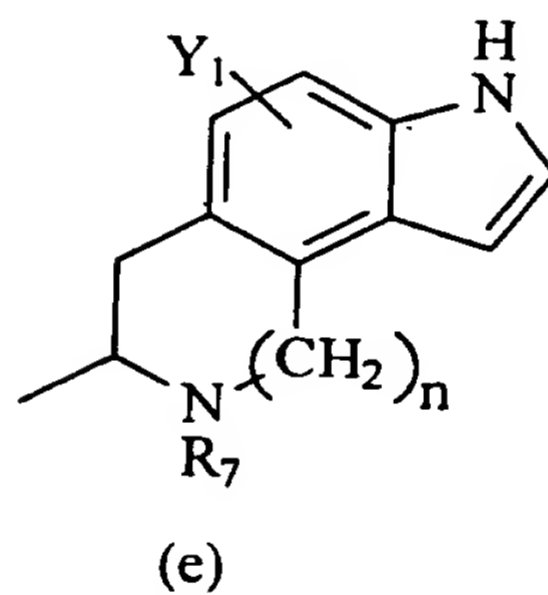
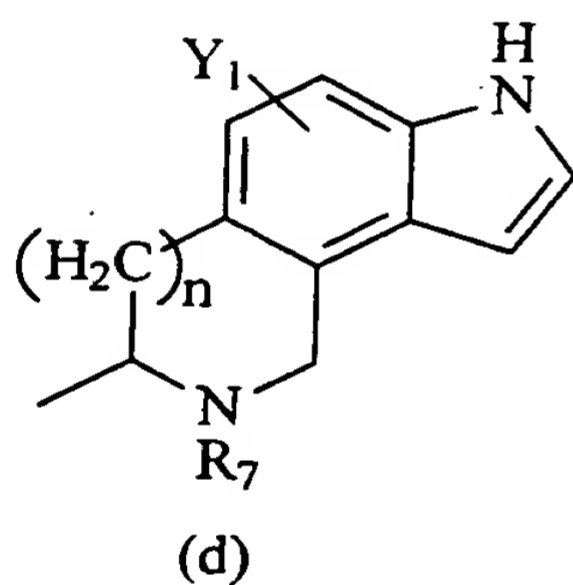
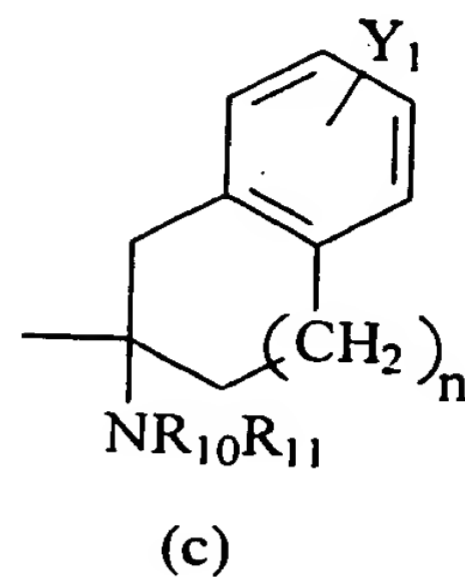
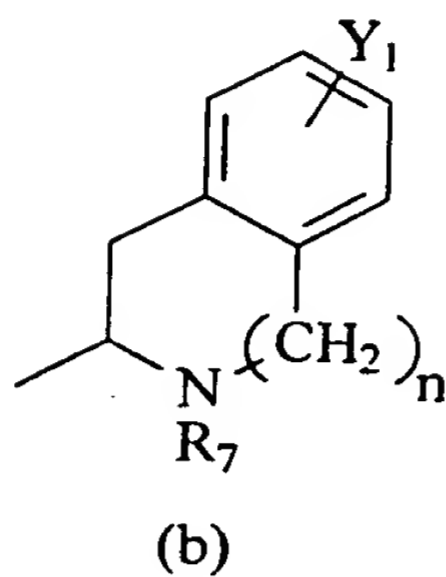
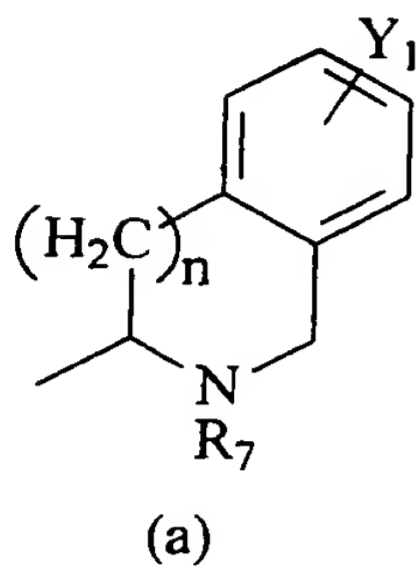
R₄ is hydrogen, C₁₋₈ alkyl, CO₂C₁₋₈ alkylaryl substituted by one or more groups Y₁,
 CH₂aryl substituted by one or more groups Y₁ or CO₂C₁₋₈ alkyl;

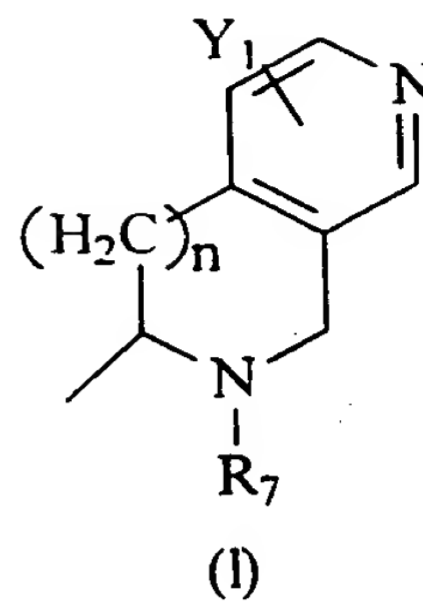
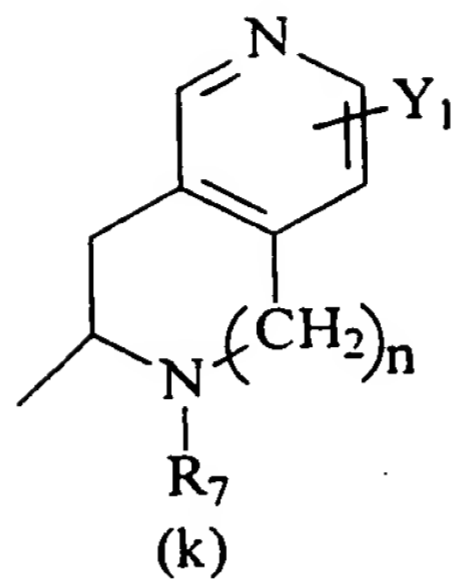
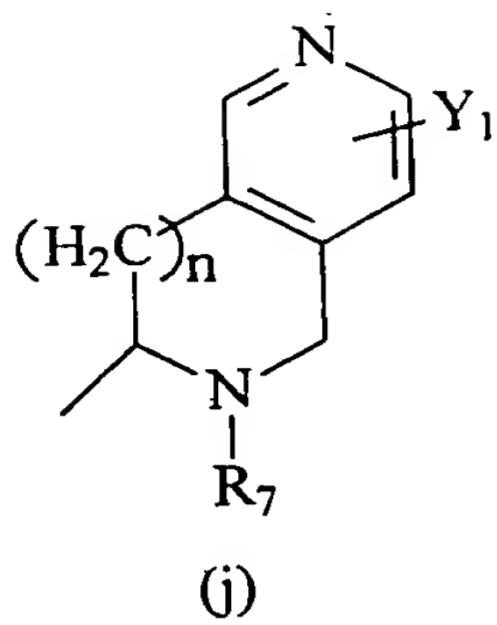
Z is N, O or S; where Z is O or S, there is no R₅

R₅ is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, CH₂CO₂C₁₋₈ alkyl, CO₂C₁₋₈ alkyl or
 CH₂aryl substituted by one or more groups Y₁;

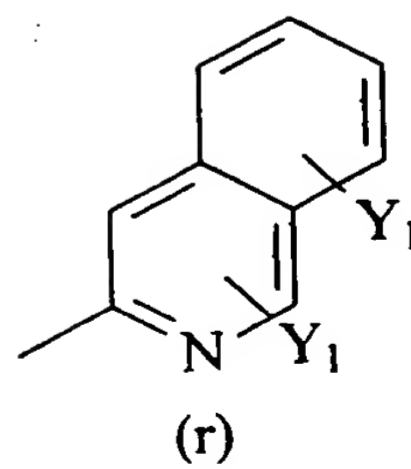
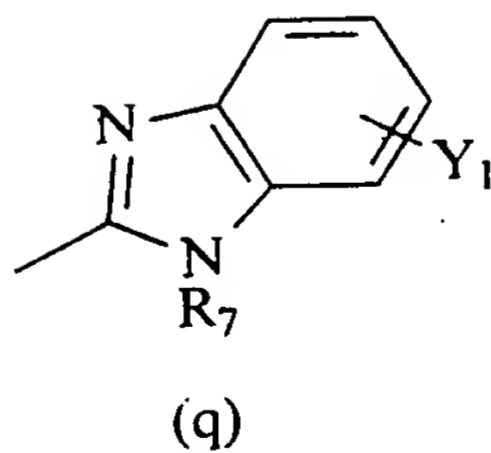
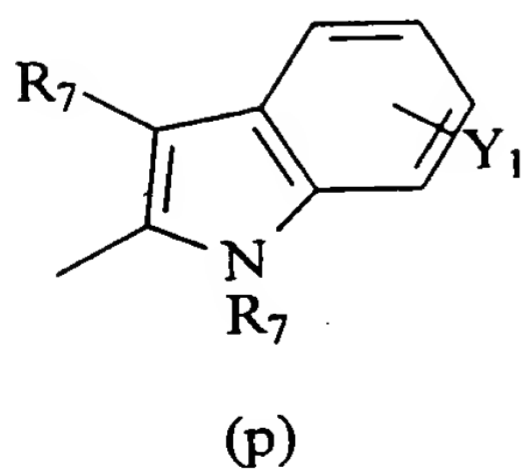
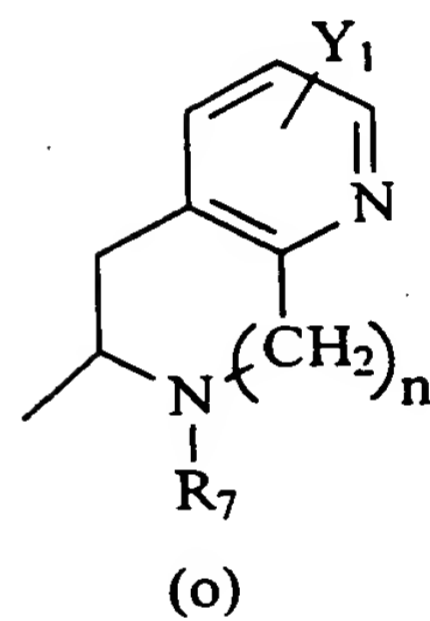
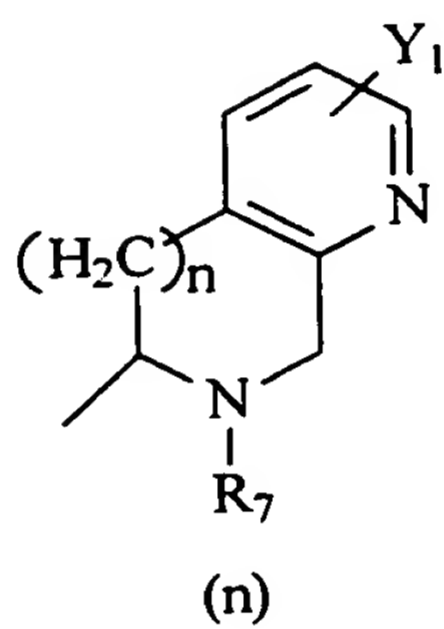
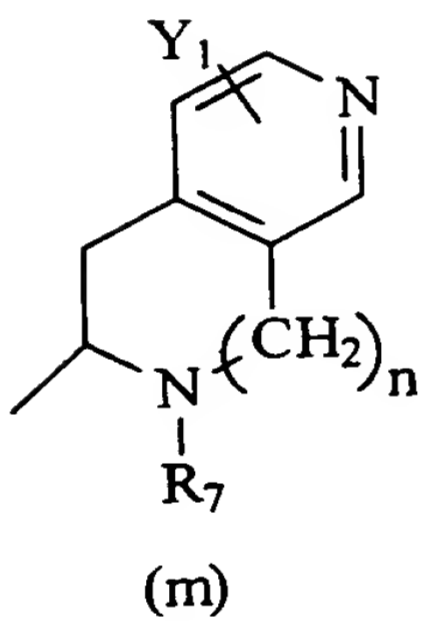
n is 0, 1, 2 or 3;

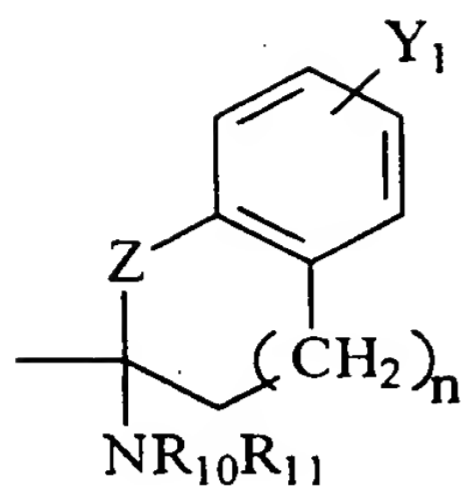
R₆ is a group selected from the group consisting of structures (a)-(bbb):



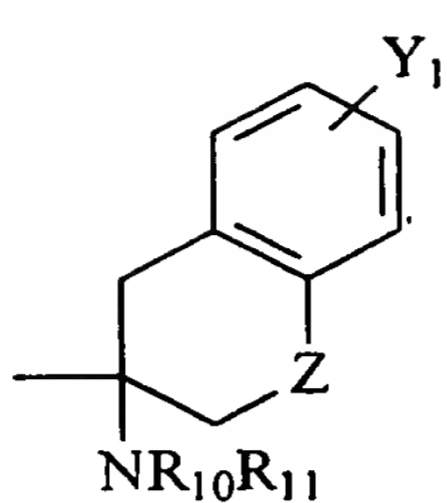


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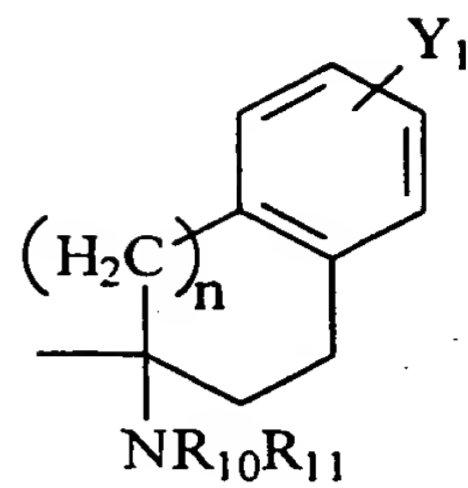




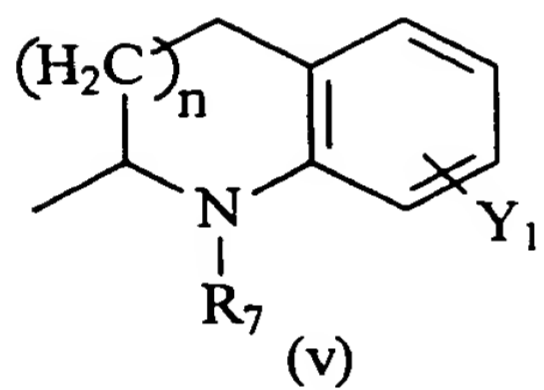
(s)



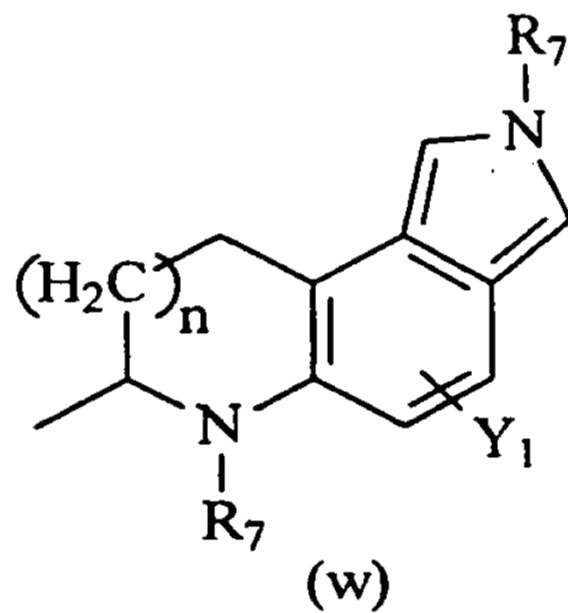
(t)



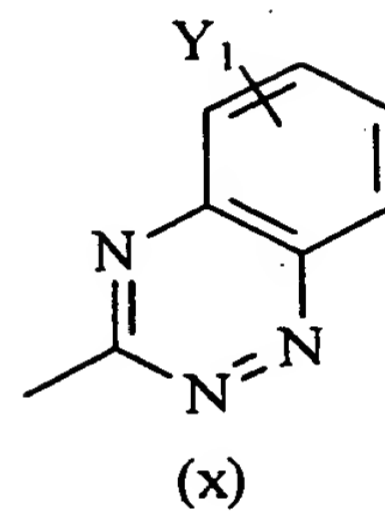
(u)



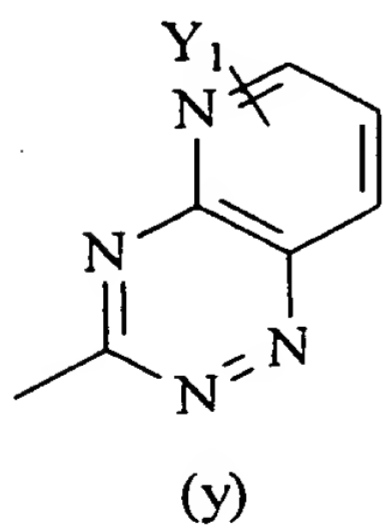
(v)



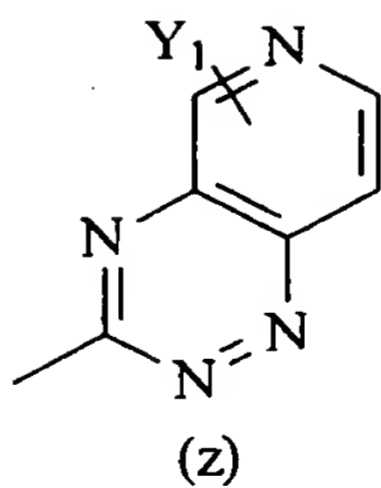
(w)



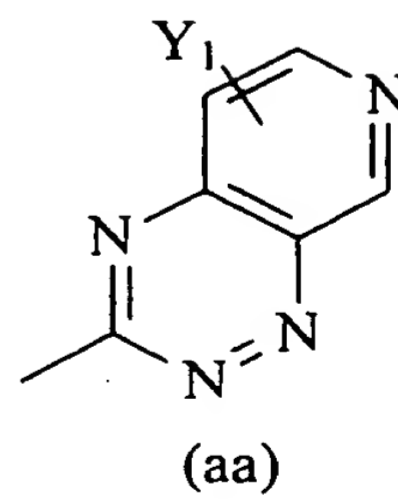
(x)



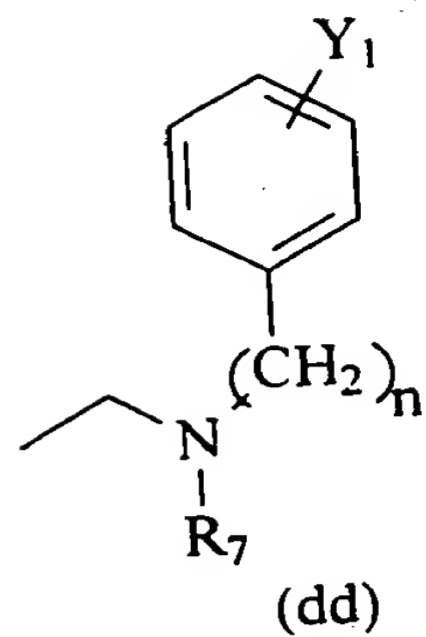
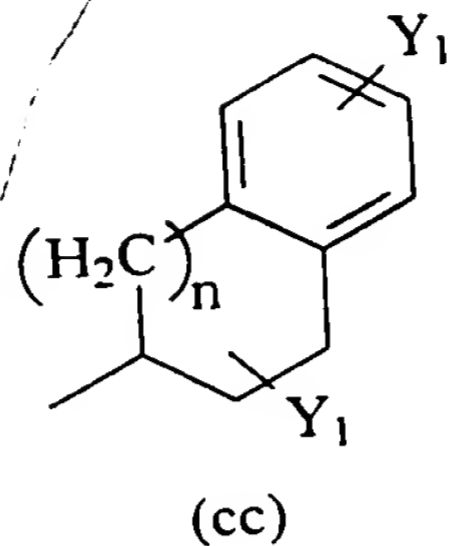
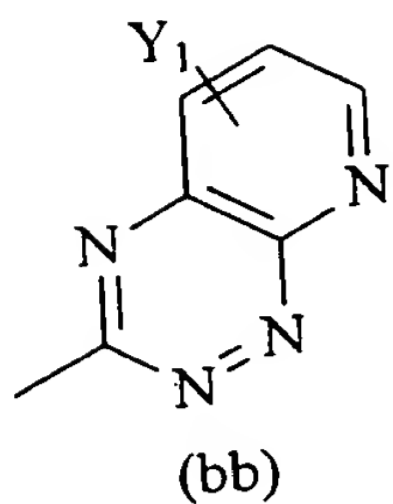
(y)



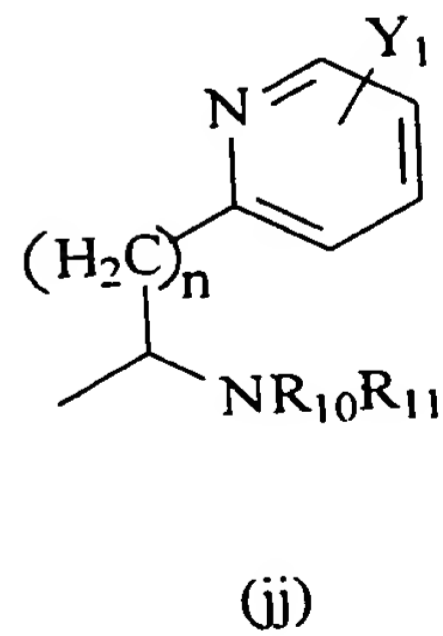
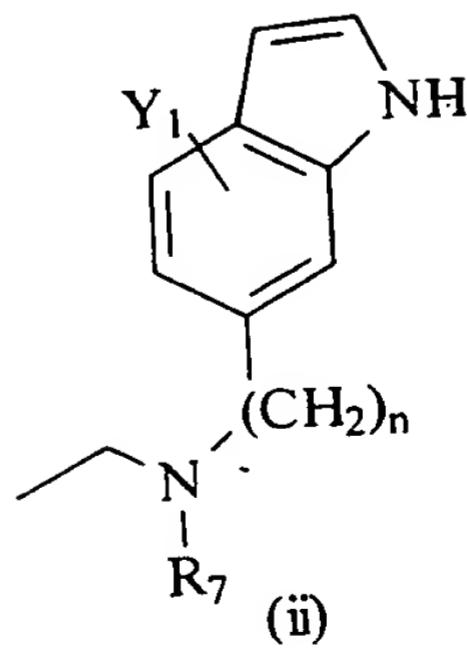
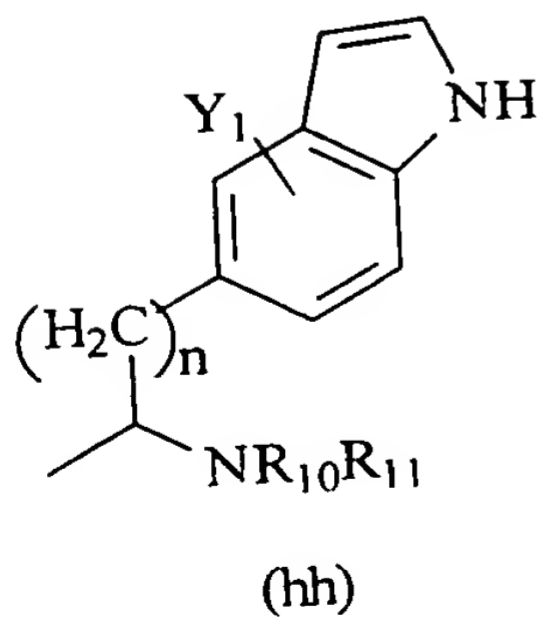
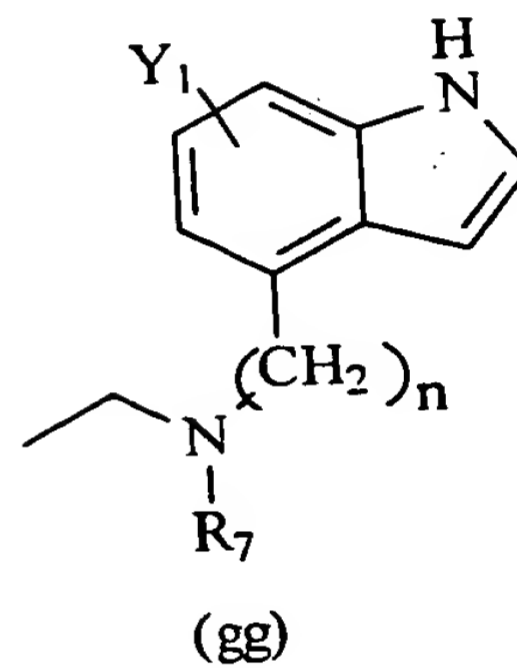
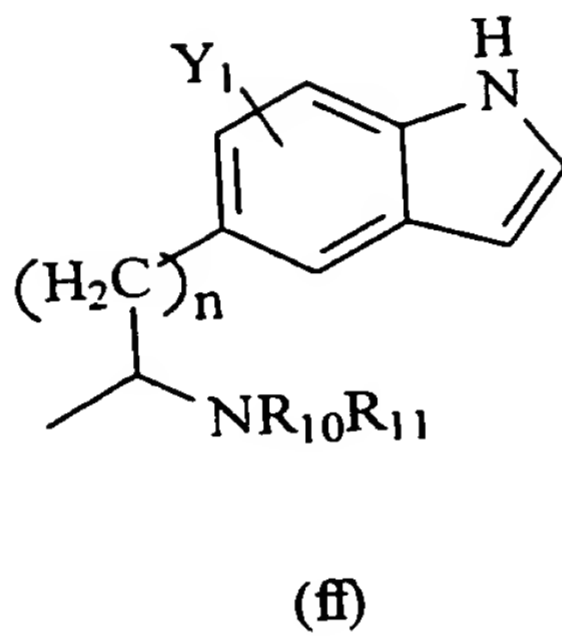
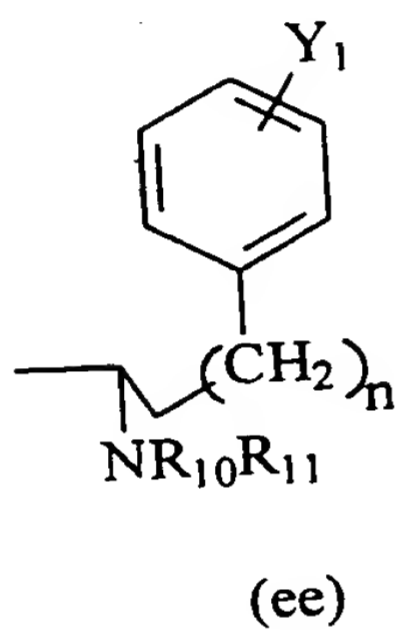
(z)

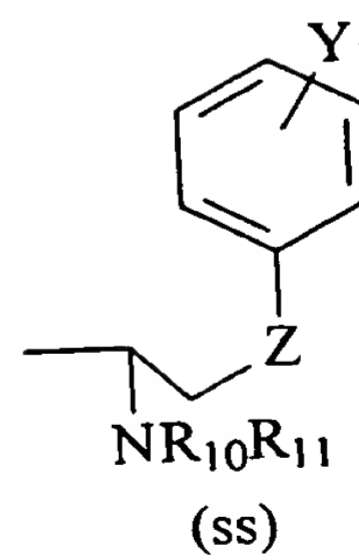
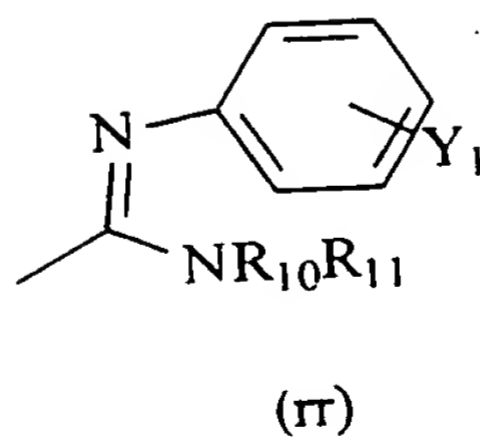
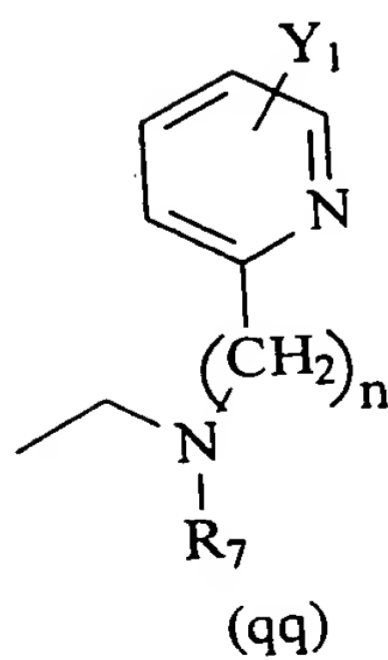
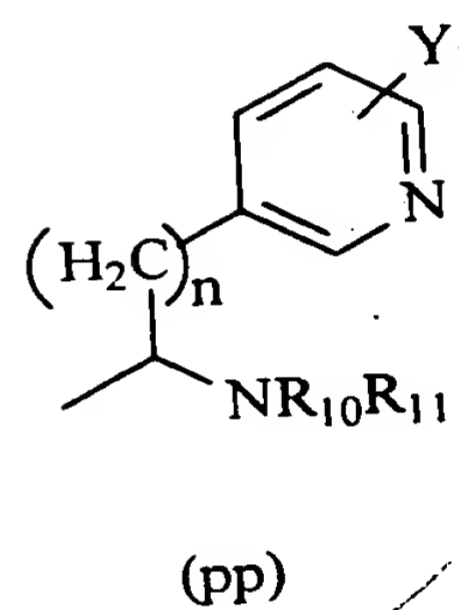
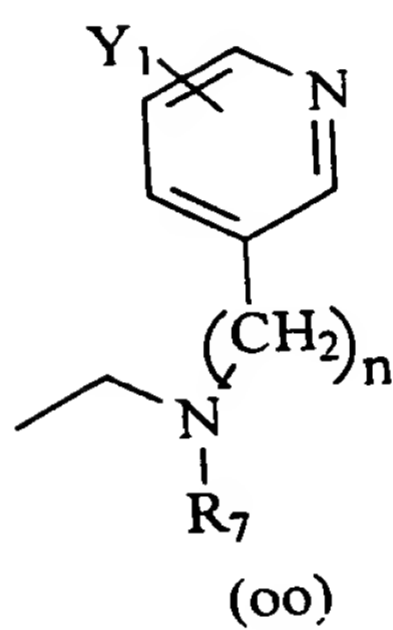
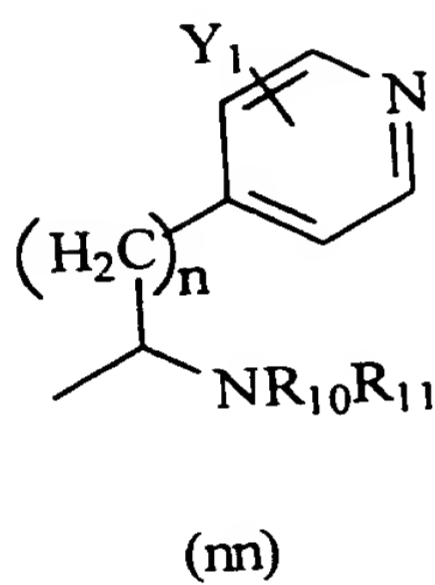
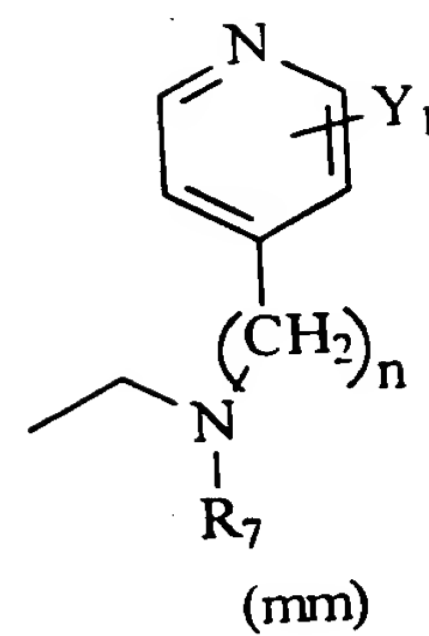
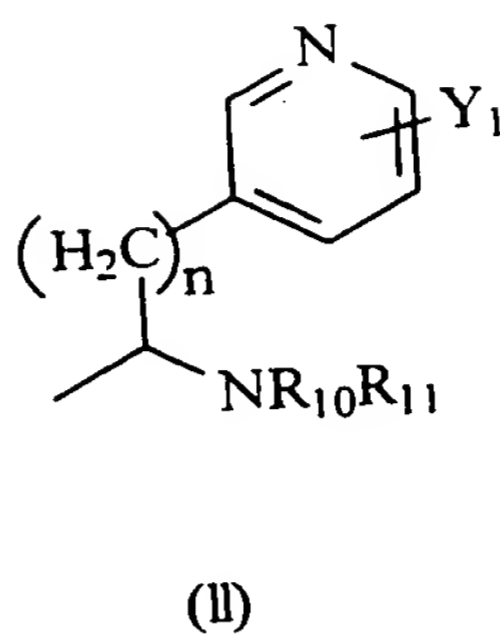
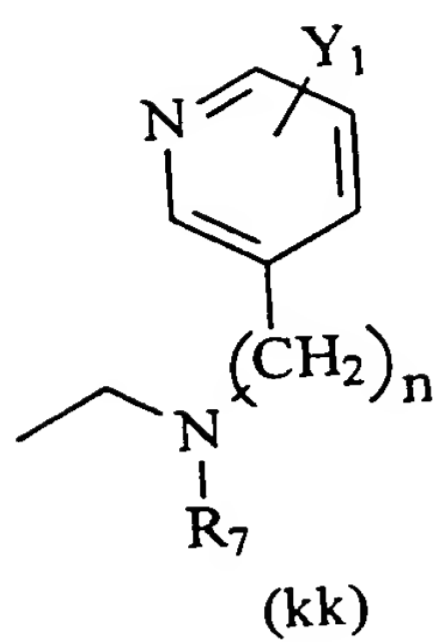


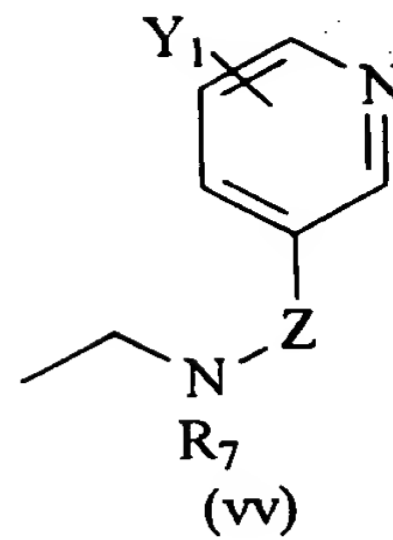
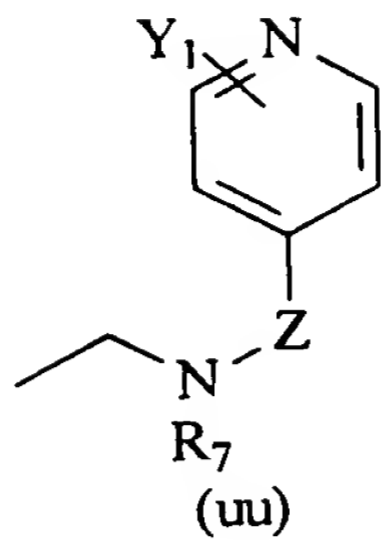
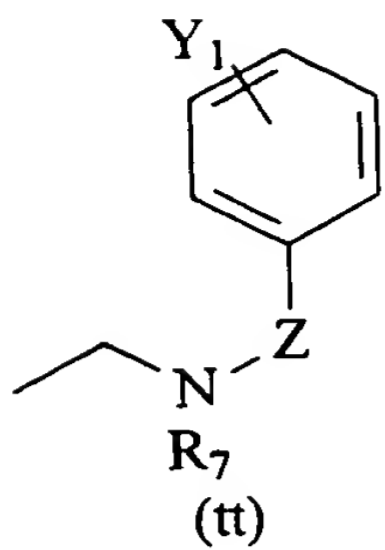
(aa)



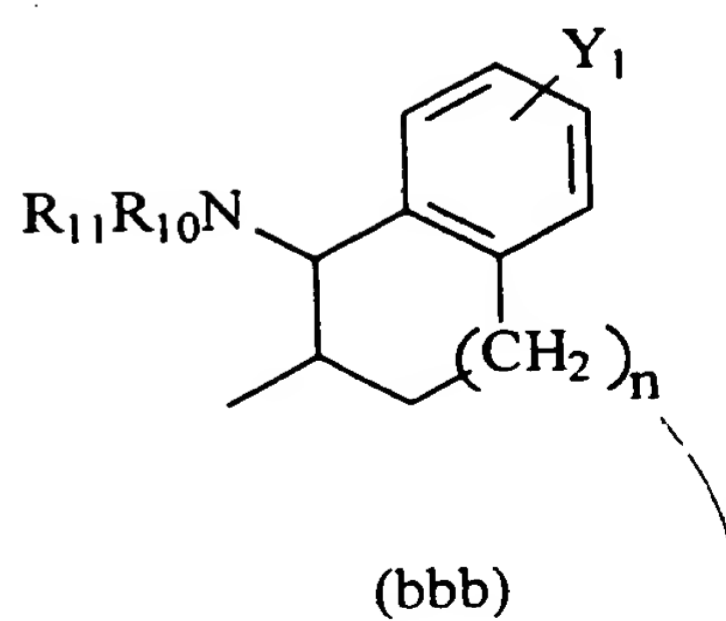
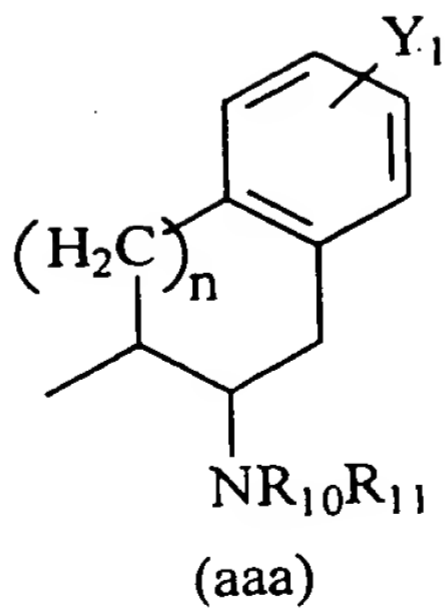
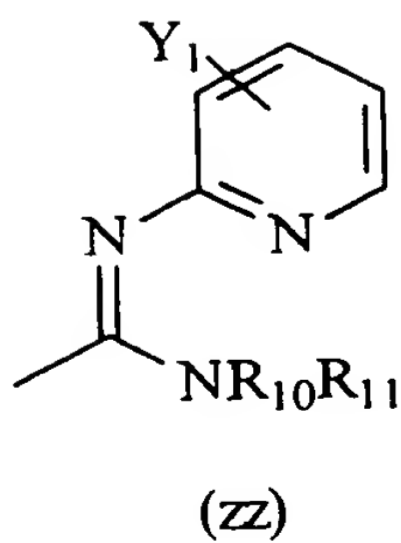
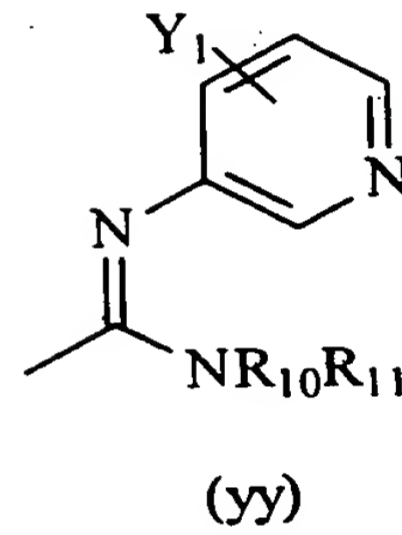
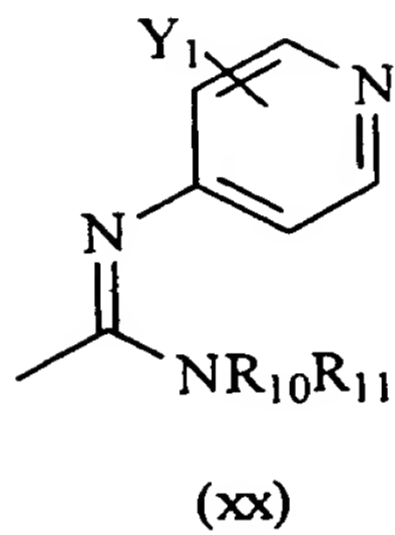
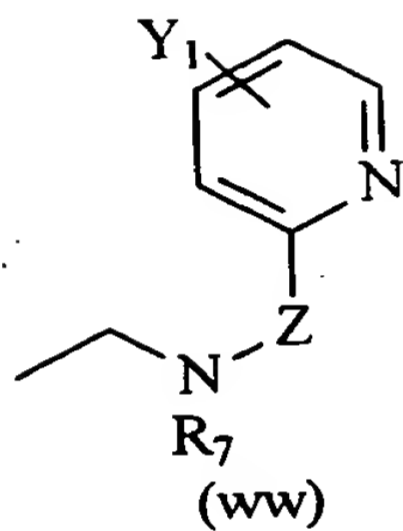
B8







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X_1 is hydrogen, C_{1-8} alkyl, C_{3-8} alkenyl, or C_{3-8} alkynyl;

X_2 is hydrogen, C_{1-8} alkyl, C_{3-8} alkenyl, or C_{3-8} alkynyl;

or X_1 and X_2 together form $=O$, $=S$, $=NH$;

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, $CH_2(CH_2)_nY_2$, or $C(=NH)NR_{16}R_{17}$;

R_8 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

R_9 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{10} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{11} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{12} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{13} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{14} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{15} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{16} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$; and

R_{17} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_n Y_2$.

2. (Currently Amended) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein R_1 , R_4 , R_5 , Y_1 , Y_2 , Z , n , X_1 , X_2 , and R_7 - R_{17} are as ~~indicated above~~ in Claim 1;

Y_3 is H;

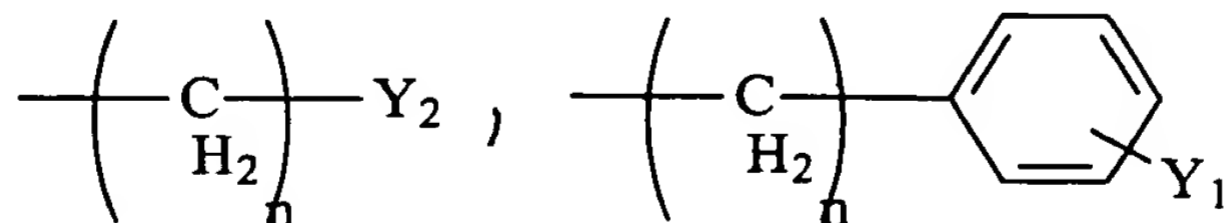
R_2 and R_3 are each, independently, H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, or CH_2 aryl substituted by one or more substituents Y_1 ; and

R_6 is a group having a formula selected from the group consisting of structures (a)-(cc):

and pharmaceutically acceptable salts thereof.

3. (Currently Amended) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I) wherein Y_1 , Y_2 , R_4 , R_5 , Z , n , X_1 , X_2 and R_8 - R_{15} are as ~~indicated above~~ in Claim 1;

R_1 is C_{1-8} alkyl, or one of the following structures:



Y_3 is H;

R_2 and R_3 are each, independently, H or C_{1-8} alkyl, wherein R_2 and R_3 cannot both be H at the same time;

R_6 is a formula selected from the structures (a)-(r); and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

4. (Currently Amended) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I) wherein Y_1 , Z, n, X_1 , X_2 and R_8 - R_{15} are as noted above in Claim 1;

R_1 is C_{1-8} alkyl;

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each, independently, H or methyl, wherein R_2 and R_3 cannot both be H at the same time;

R_4 is H, C_{1-8} alkyl, CO_2C_{1-8} alkyl, ~~aryl~~ or CH_2 aryl substituted by one or more substituents Y_1 and the stereocenter adjacent to R_4 is in an (S) configuration;

R_5 is H, C_{1-8} alkyl, or $CH_2CO_2C_{1-8}$ alkyl;

R_6 is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

5. (Currently Amended) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y_1 , Z, n, X_1 , X_2 and R_8 - R_{14} are as indicated above in Claim 1;

R_1 is methyl,

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each H or methyl, such that when R_2 is H, R_3 is methyl and vice versa;

R_4 is C_{1-8} alkyl, or CO_2C_{1-8} alkyl, and the stereocenter adjacent to R_4 has a configuration of (S);

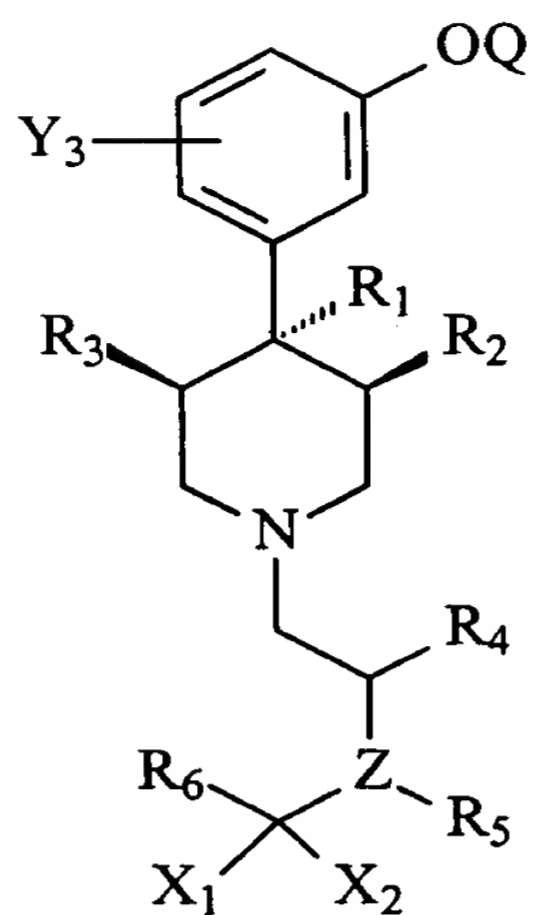
R_5 is H;

R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 or $CH_2(CH_2)_nY_2$.

6. (Original) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound selected from formulae 14-21 of Fig. 1.

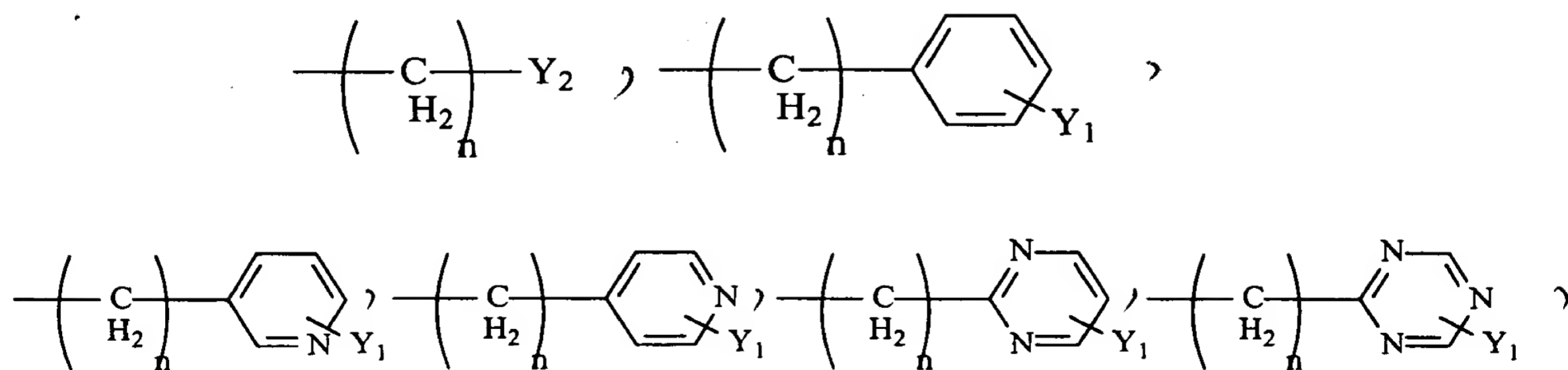
7. (Currently Amended) A kappa opioid receptor antagonist compound represented by the formula (I):



(I)

wherein Q is H or COC₁₋₈ alkyl;

R₁ is C₁₋₈ alkyl, or one of the following structures:



Y_1 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

R_2 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 ;

R_3 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 ;

wherein R_2 and R_3 may be bonded together to form a C_{2-8} alkyl group;

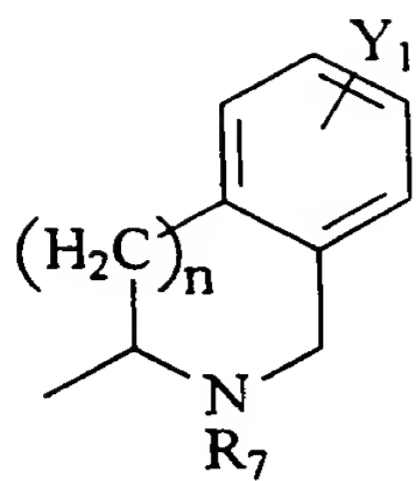
R_4 is hydrogen, C_{1-8} alkyl, CO_2C_{1-8} alkylaryl substituted by one or more groups Y_1 , CH_2 aryl substituted by one or more groups Y_1 or CO_2C_{1-8} alkyl;

Z is N, O or S; when Z is O or S there is no R_5

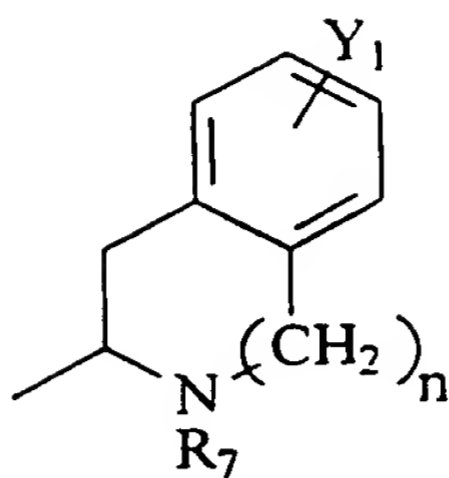
R_5 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $CH_2CO_2C_{1-8}$ alkyl, CO_2C_{1-8} alkyl or CH_2 aryl substituted by one or more groups Y_1 ;

n is 0, 1, 2 or 3;

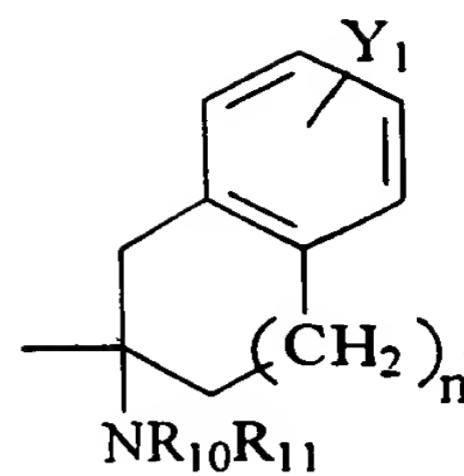
R_6 is a group selected from the group consisting of structures (a)-(bbb):



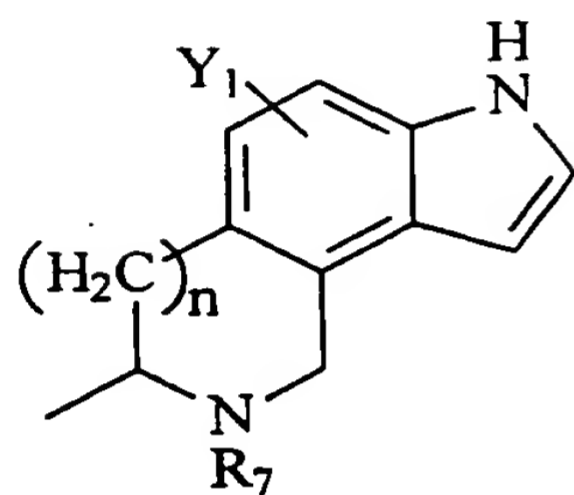
(a)



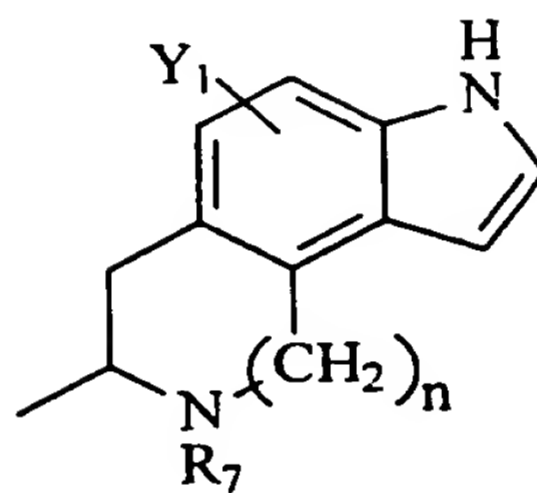
(b)



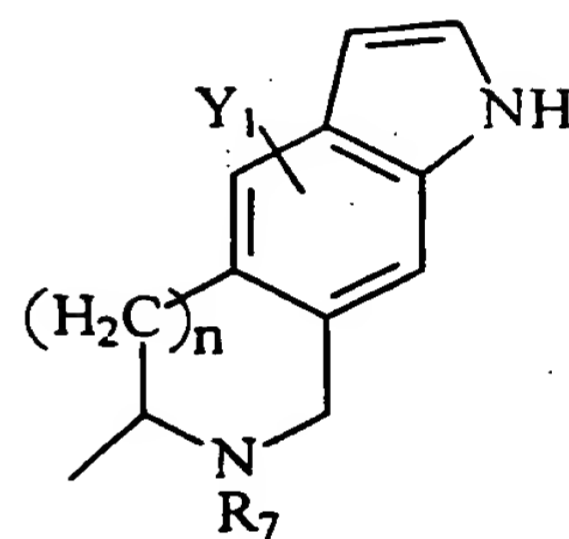
(c)



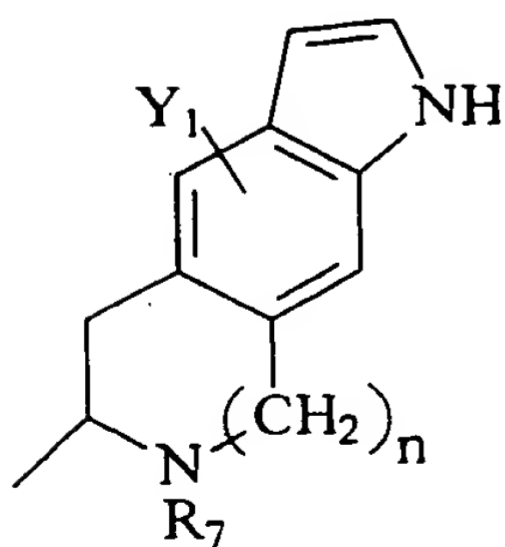
(d)



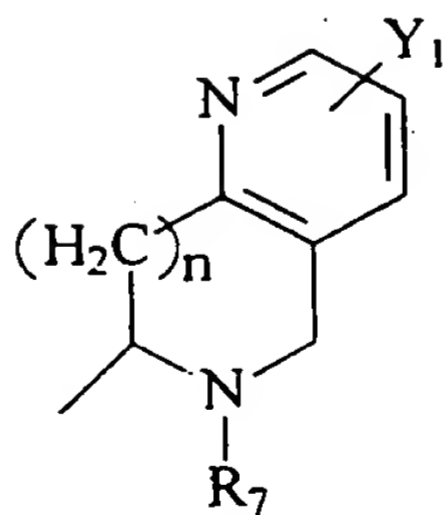
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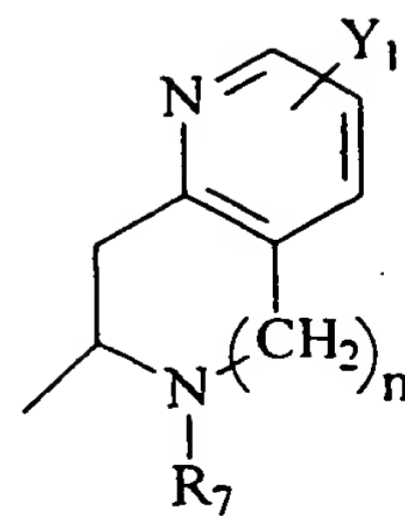
(f)



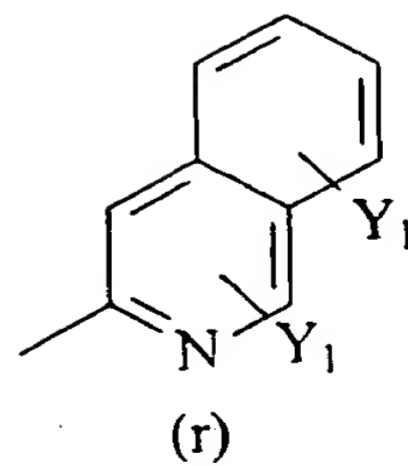
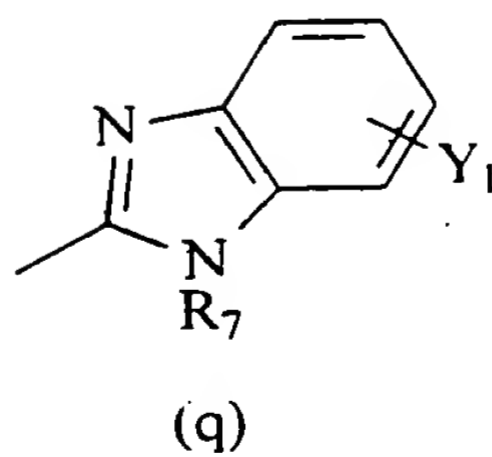
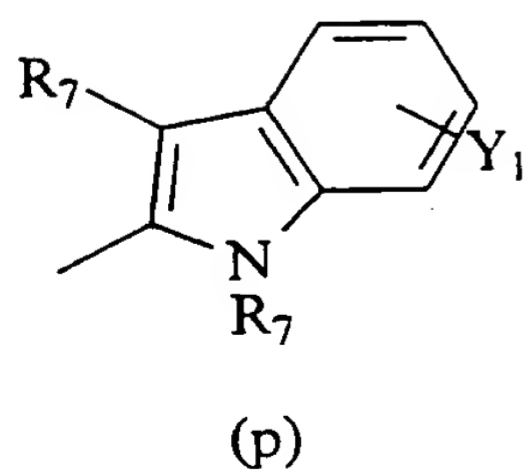
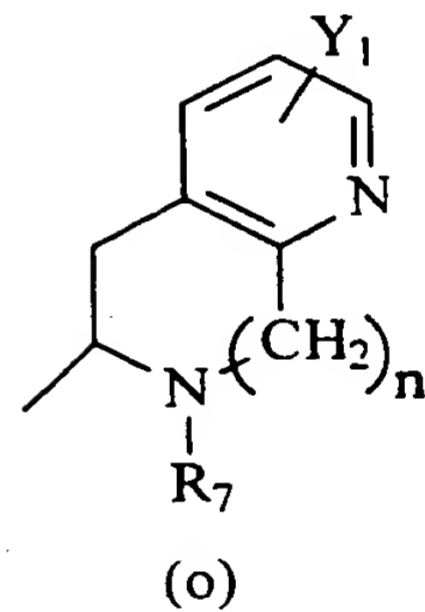
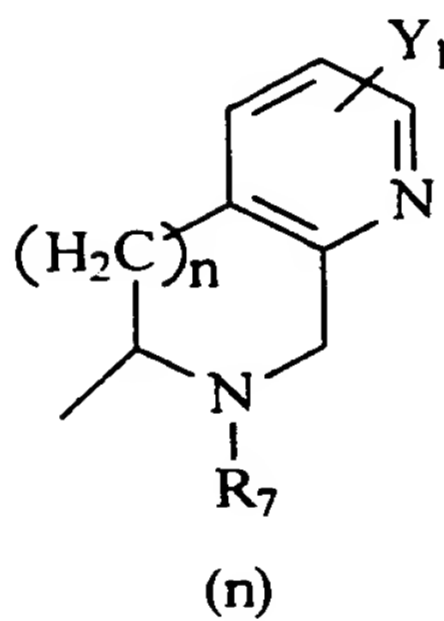
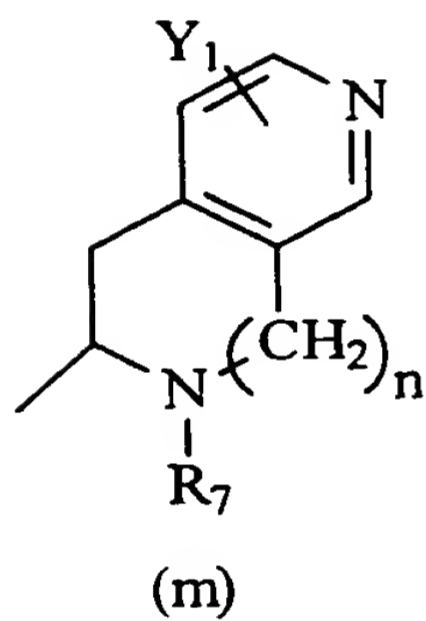
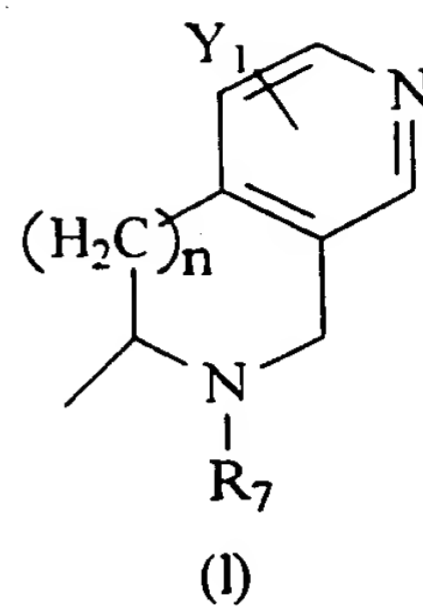
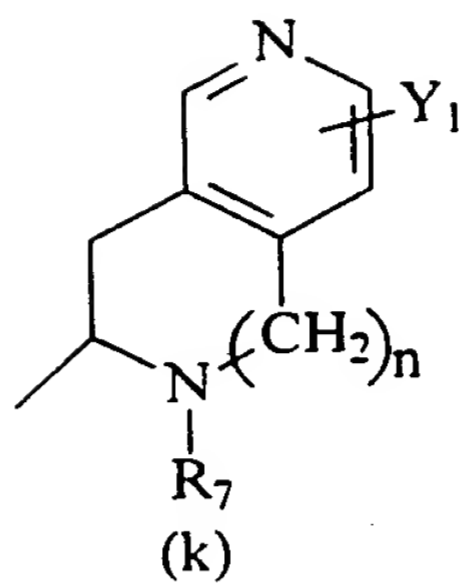
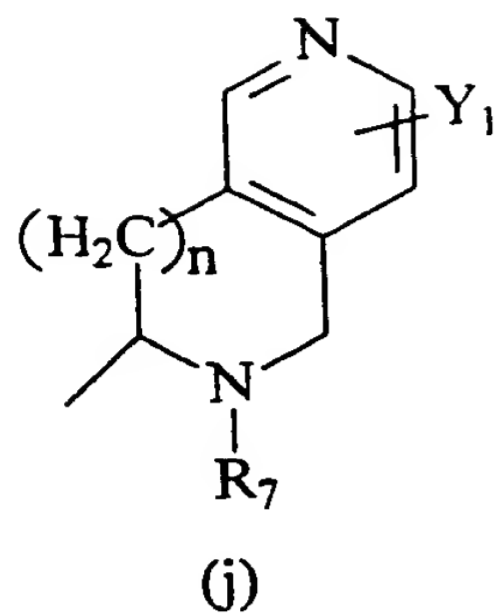
(g)

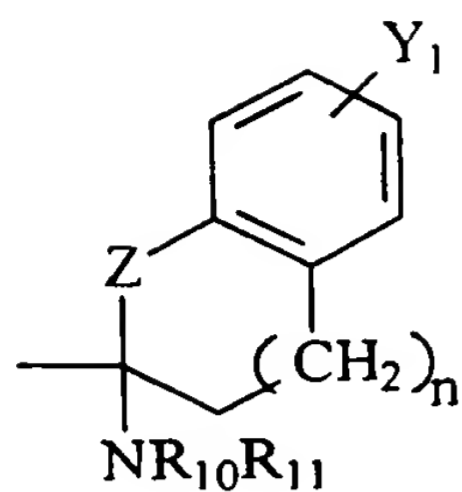


(h)

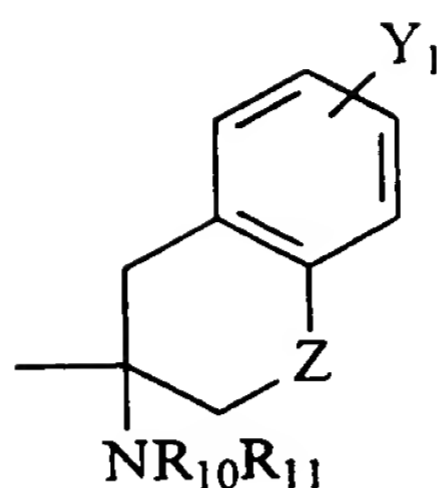


(i)

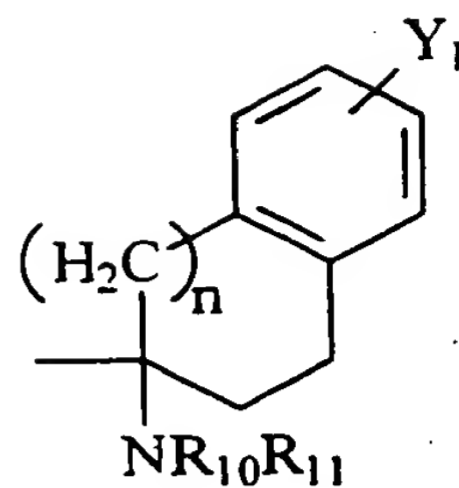




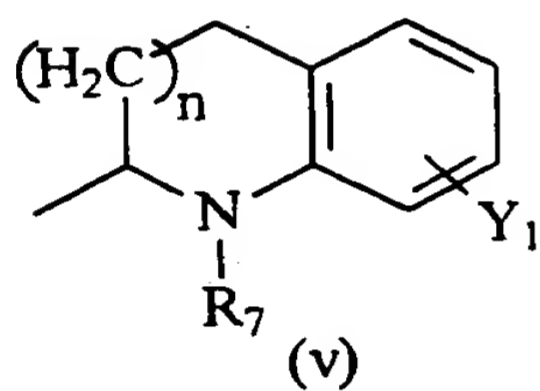
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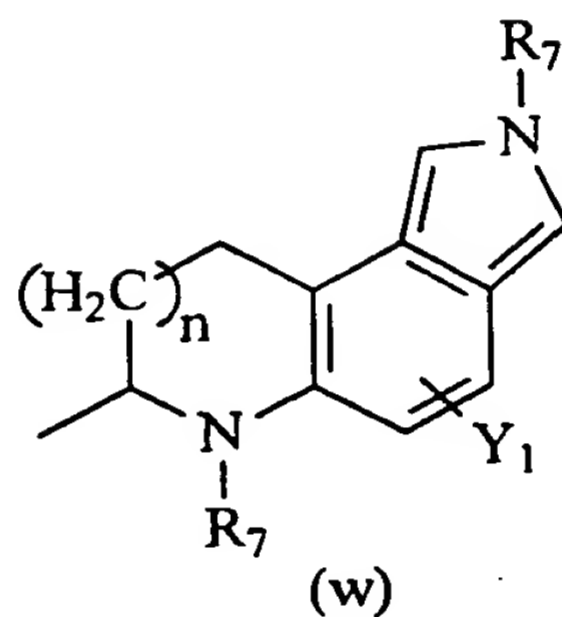
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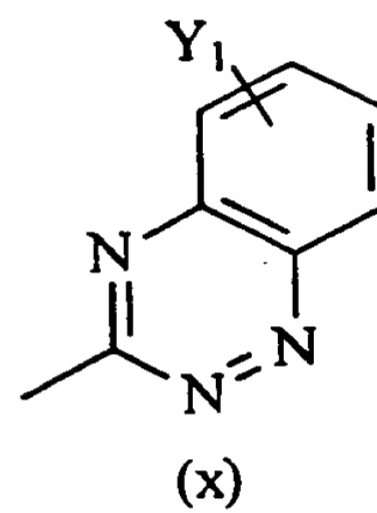
(u)



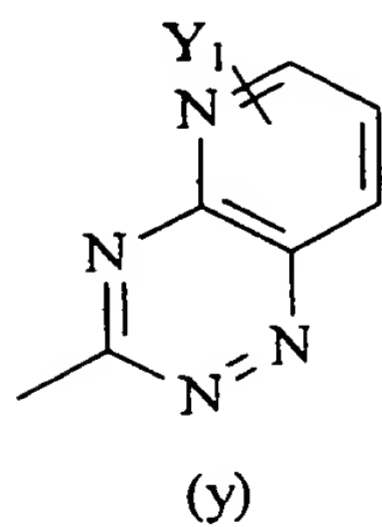
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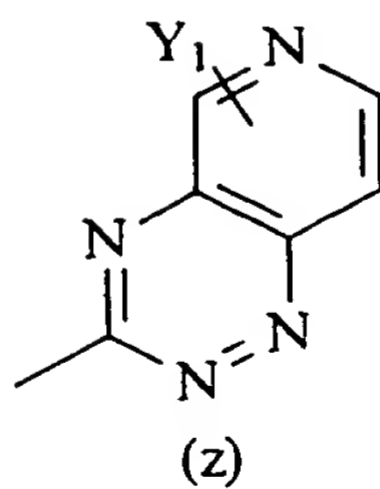
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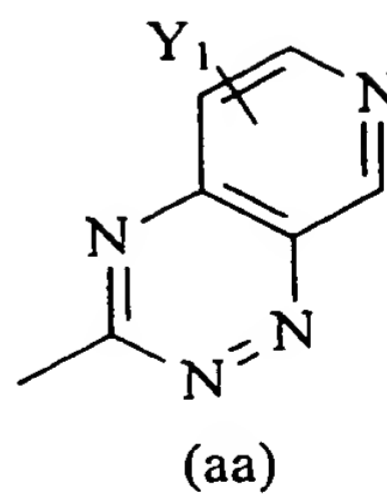
(x)



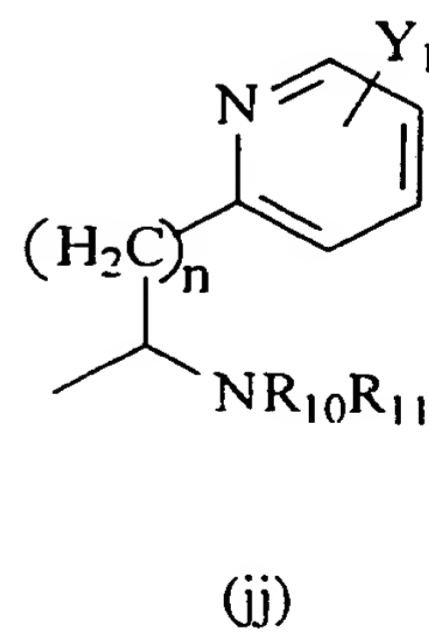
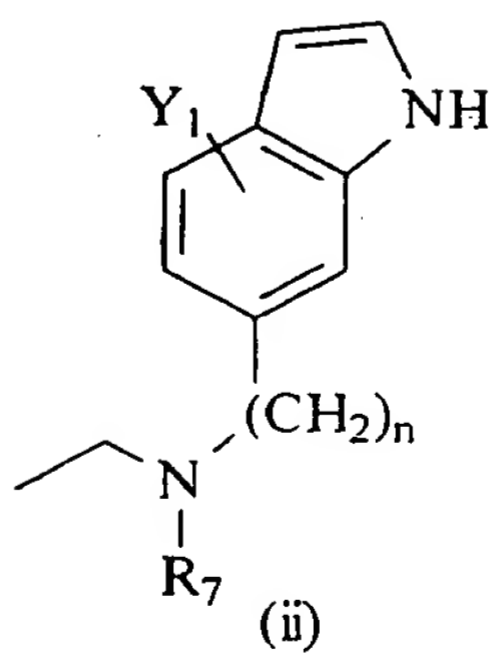
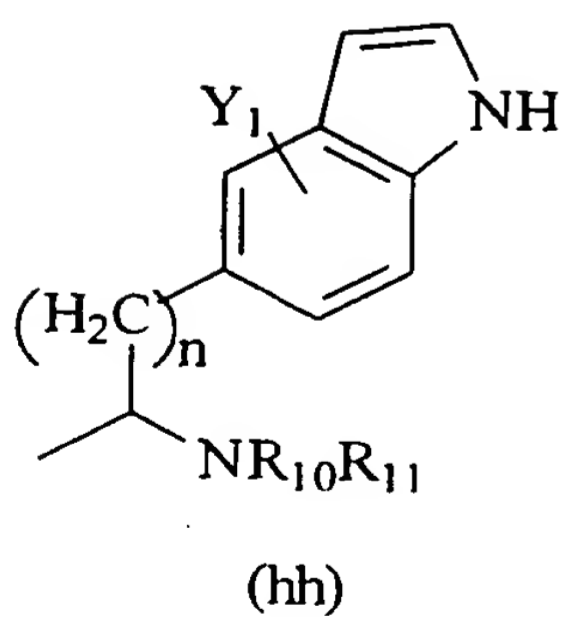
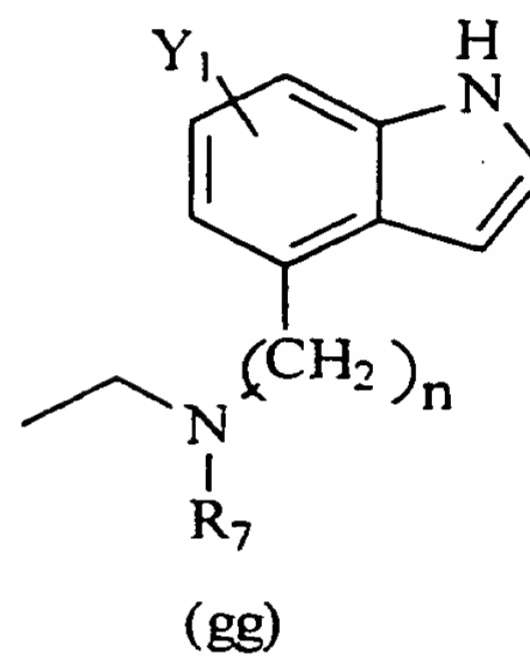
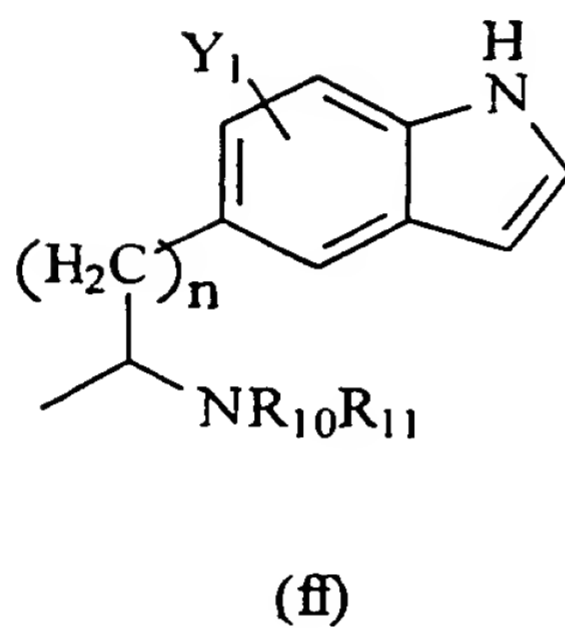
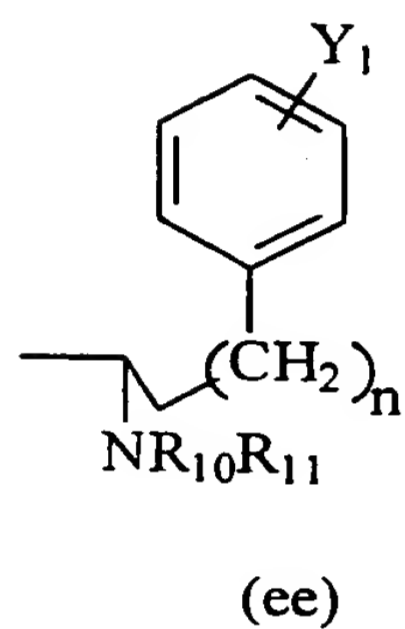
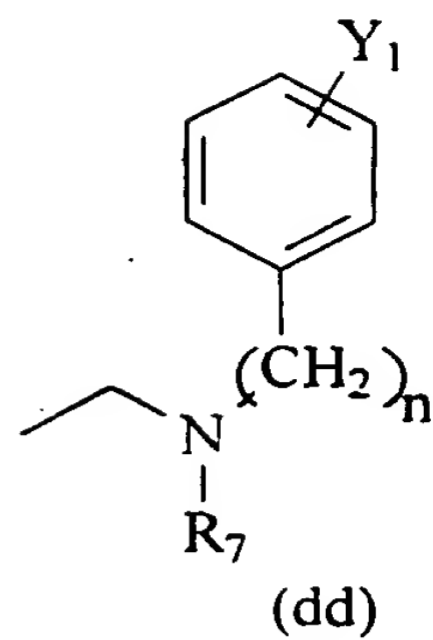
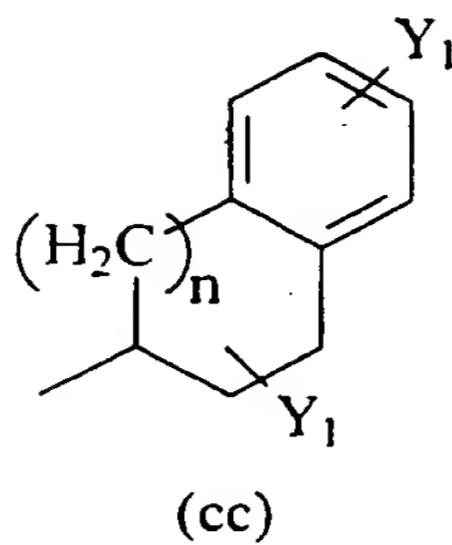
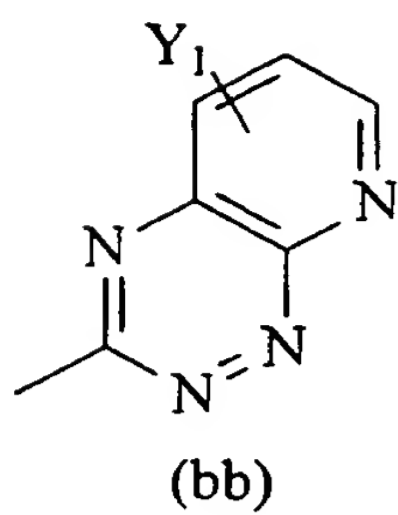
(y)

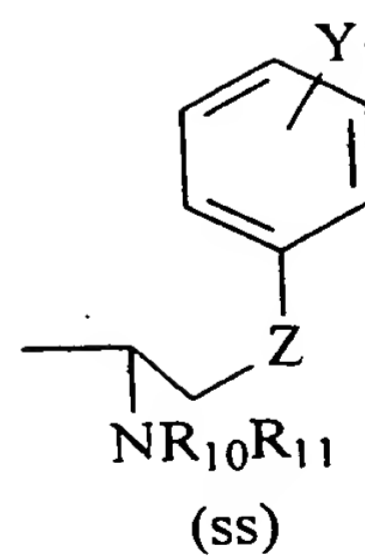
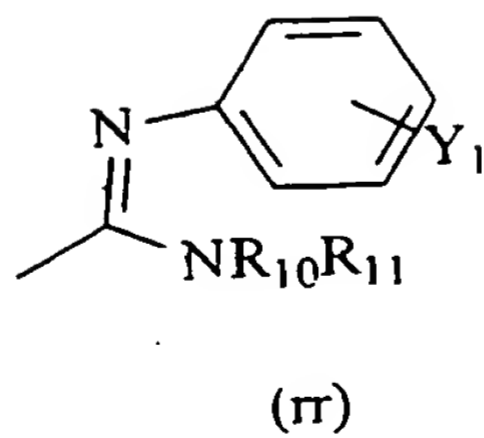
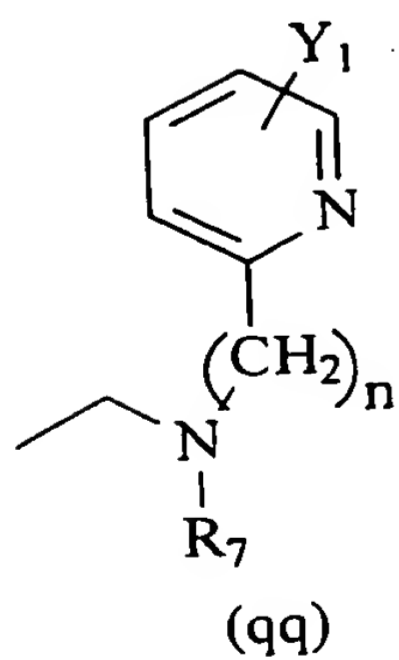
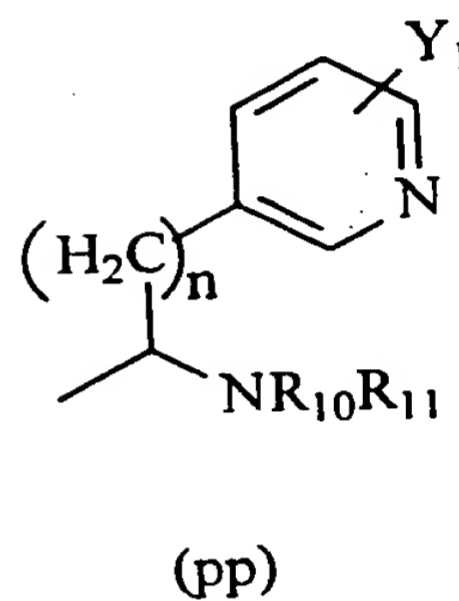
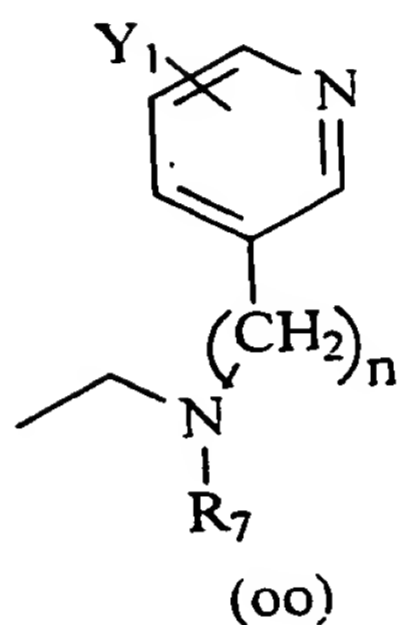
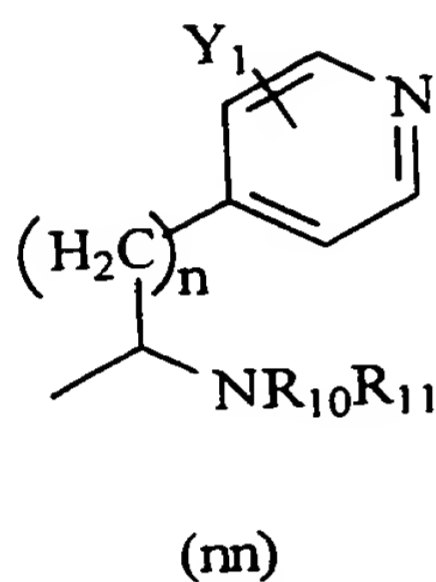
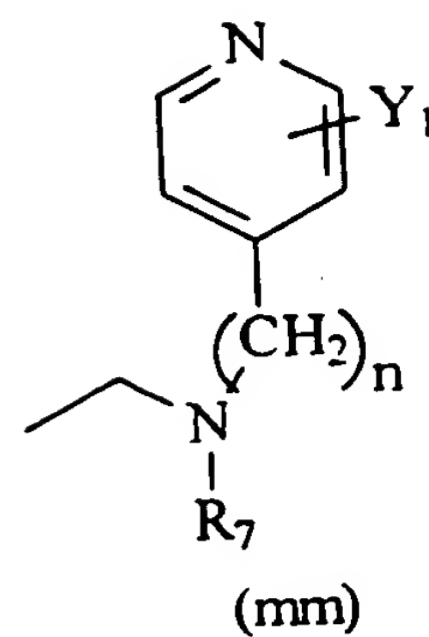
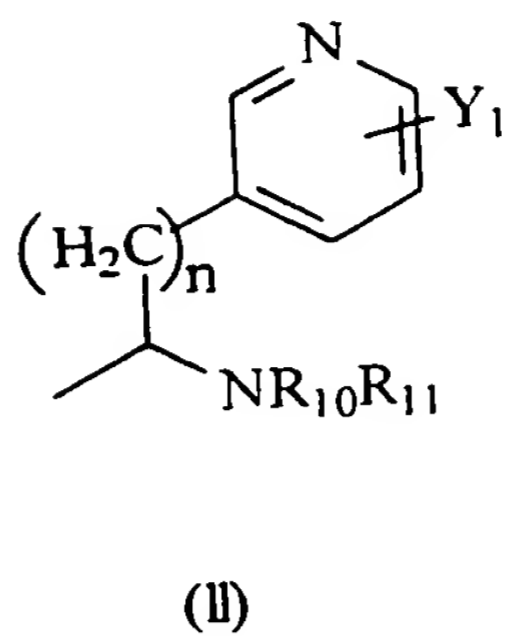
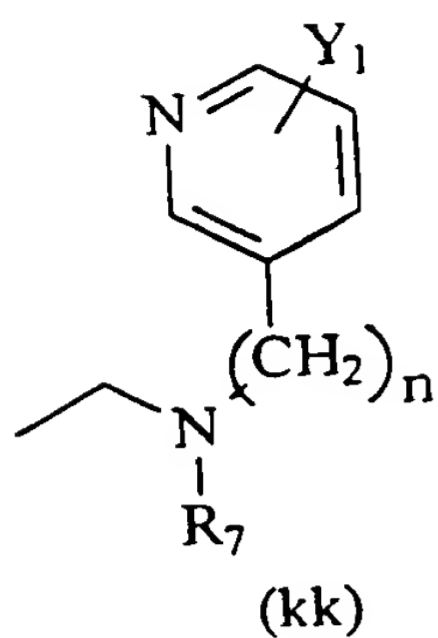


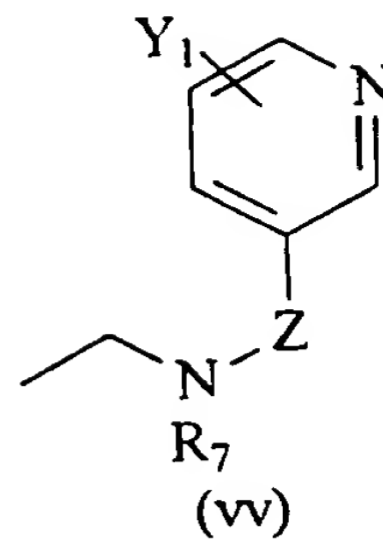
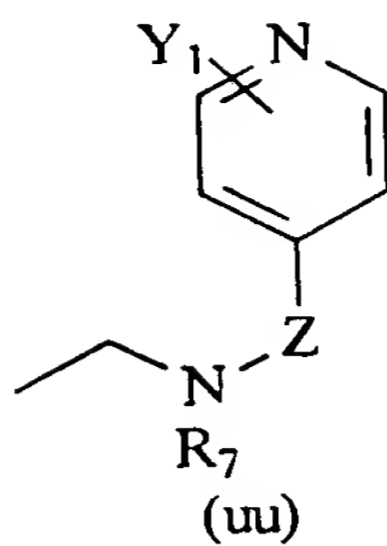
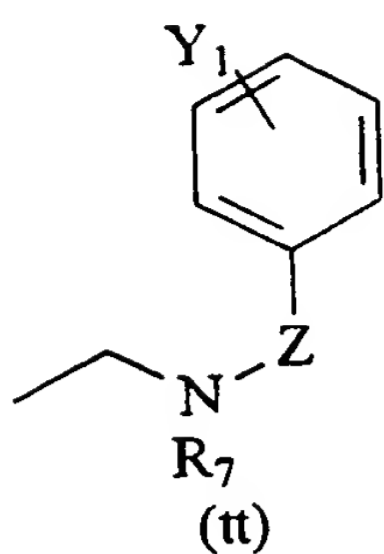
(z)



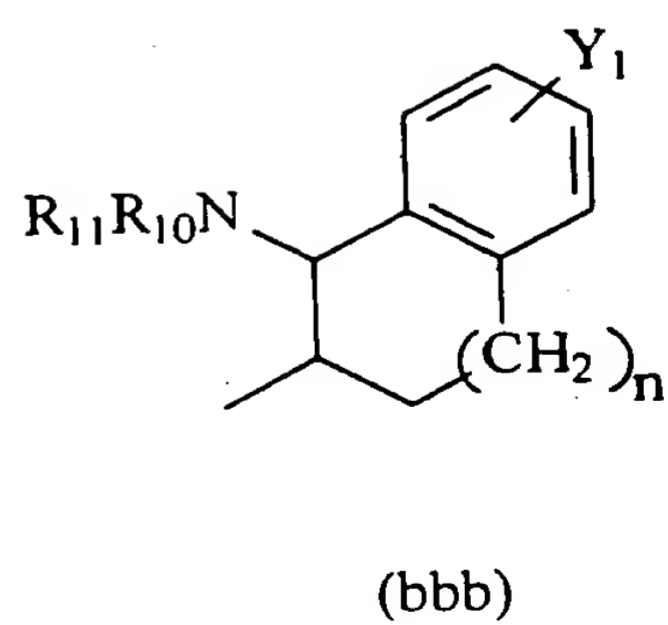
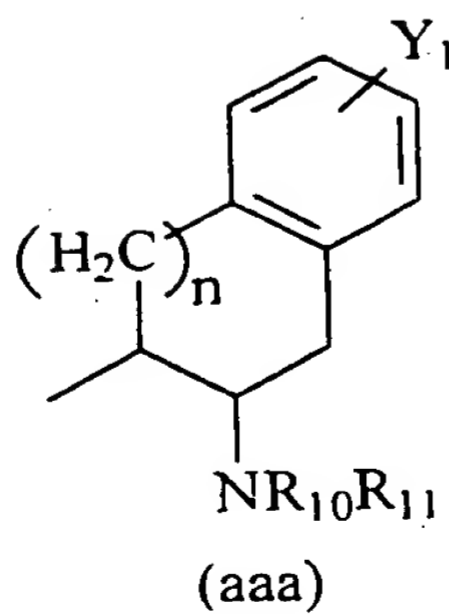
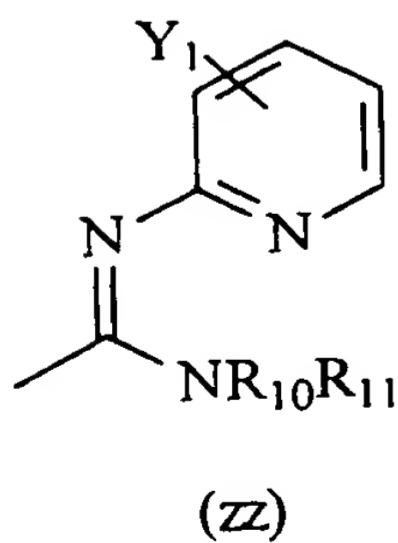
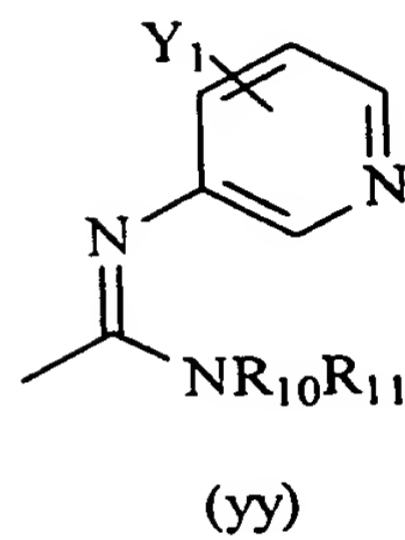
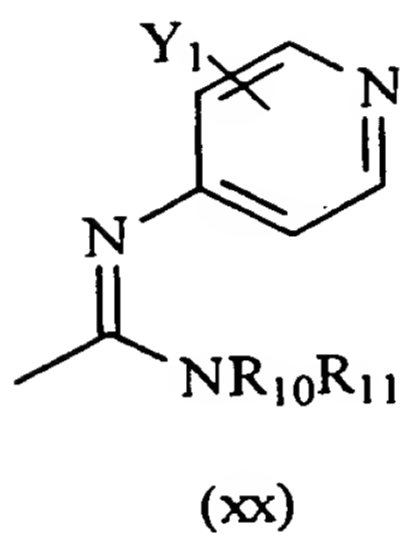
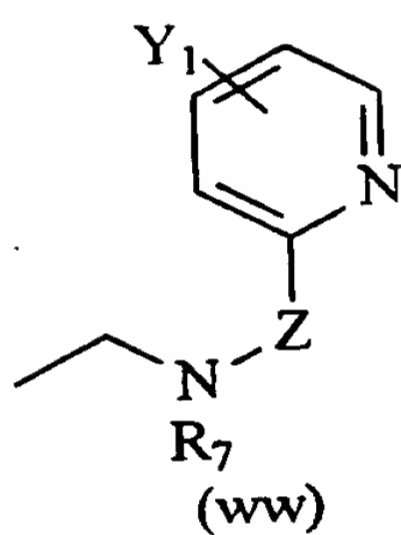
(aa)







B8



X_1 is hydrogen, C_{1-8} alkyl, C_{3-8} alkenyl, or C_{3-8} alkynyl;

X_2 is hydrogen, C_{1-8} alkyl, C_{3-8} alkenyl, or C_{3-8} alkynyl;

or X_1 and X_2 together form $=O$, $=S$, or $=NH$;

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, $CH_2(CH_2)_nY_2$, or $C(=NH)NR_{16}R_{17}$;

R_8 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

R_9 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{10} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{11} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{12} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{13} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{14} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{15} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{16} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$; and

R₁₇ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, or
CH₂(CH₂)_nY₂

and pharmaceutically acceptable salts thereof.

8. (Currently Amended) The kappa opioid receptor antagonist compound of claim 7,
wherein R₁, R₄, R₅, Y₁, Y₂, Z, n, X₁, X₂, and R₇-R₁₇ are as ~~indicated above~~ in Claim 7;

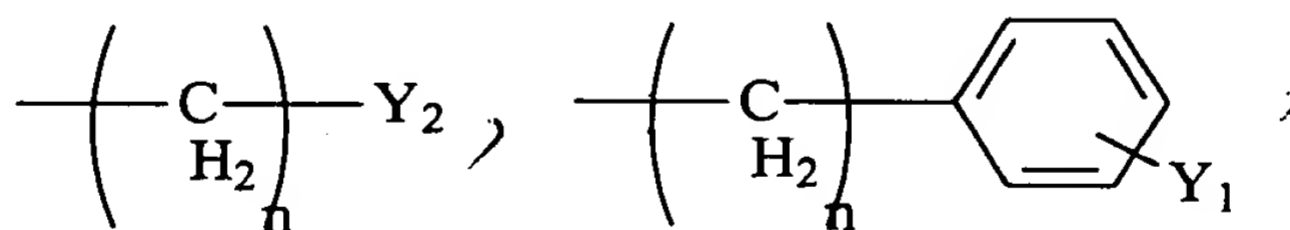
Y₃ is H;

R₂ and R₃ are each, independently, H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, or CH₂aryl
substituted by one or more substituents Y₁; and

B8 R₆ is a group having a formula selected from the group consisting of structures (a)-
(cc).

9. (Currently Amended) The kappa opioid receptor antagonist compound of claim 7,
wherein Y₁, Y₂, R₄, R₅, Z, n, X₁, X₂ and R₈-R₁₅ are as ~~indicated above~~ in Claim 7;

R₁ is C₁₋₈ alkyl, or one of the following structures:



Y₃ is H;

R₂ and R₃ are each, independently, H or C₁₋₈ alkyl, wherein R₂ and R₃ cannot both be
H at the same time;

R₆ is a formula selected from the structures (a)-(r) ~~shown above~~; and

R₇ is H, C₁₋₈ alkyl, CH₂aryl substituted by one or more substituents Y₁, NR₁₀R₁₁,
NHCOR₁₂, NHCO₂R₁₃, CONR₁₄R₁₅, or CH₂(CH₂)_nY₂.

10. (Currently Amended) The kappa opioid receptor antagonist compound of claim 7,
wherein Y₁, Z, n, X₁, X₂ and R₈-R₁₅ are as ~~noted above~~ in Claim 7;

R₁ is C₁₋₈ alkyl;

Y₂ is H, CF₃, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, CH₂OH,
CH₂OR₈, or COCH₂R₉;

Y₃ is H;

B 8 R₂ and R₃ are each, independently, H or methyl, wherein R₂ and R₃ cannot both be H
at the same time;

R₄ is H, C₁₋₈ alkyl, CO₂C₁₋₈alkyl, ~~aryl~~ or CH₂aryl substituted by one or more
substituents Y₁ and the stereocenter adjacent to R₄ is in an (S) configuration;

R₅ is H, C₁₋₈ alkyl, CH₂CO₂C₁₋₈ alkyl;

R₆ is a group having a formula selected from the group consisting of structures (a)-(c)
and (h)-(o); and

R₇ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents Y₁, NR₁₀R₁₁,
NHCOR₁₂, NHCO₂R₁₃, CONR₁₄R₁₅, or CH₂(CH₂)_nY₂.

11. (Currently Amended) The kappa opioid receptor antagonist compound of claim 7,
wherein Y₁, Z, n, X₁, X₂ and R₈-R₁₄ are as ~~indicated above~~ in Claim 7;

R₁ is methyl,

Y₂ is H, CF₃, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄,
CH₂OH, CH₂OR₈, or COCH₂R₉;

Y_3 is H;

R_2 and R_3 are each H or methyl, such that when R_2 is H, R_3 is methyl and vice versa;

R_4 is C_{1-8} alkyl, or CO_2C_{1-8} alkyl, and the stereocenter adjacent to R_4 has a configuration of (S);

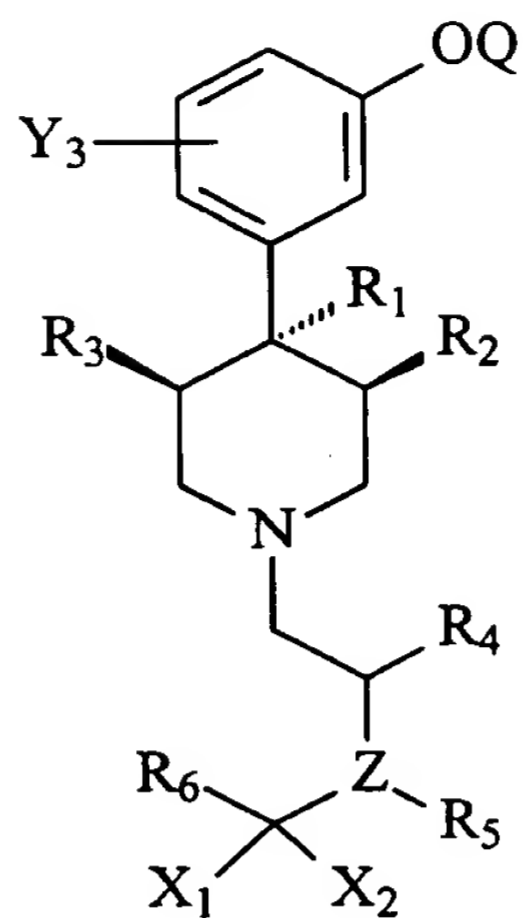
R_5 is H;

R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 or $CH_2(CH_2)_nY_2$.

12. (Original) The kappa opioid receptor antagonist of claim 7, wherein said compound is a compound selected from formulae 14-21 of Fig. 1.

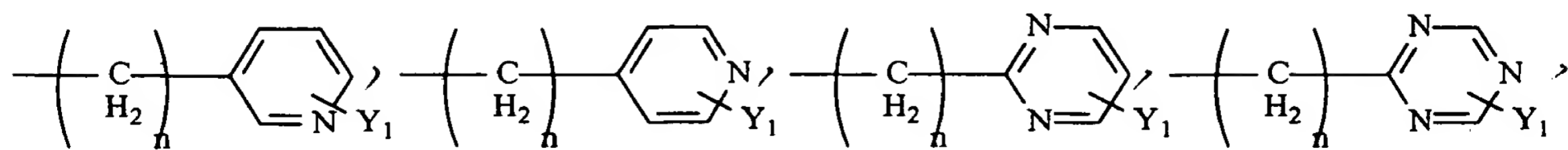
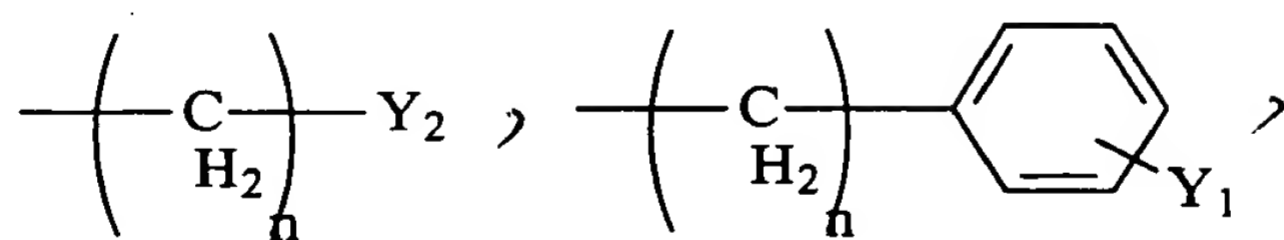
13. (Currently Amended) A pharmaceutical composition comprising:
an effective amount of a kappa opioid receptor antagonist and a physiologically acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula (I):



(I)

wherein Q is H or COC₁₋₈ alkyl;

R₁ is C₁₋₈ alkyl, or one of the following structures:



Y_1 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

R_2 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 ;

R_3 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 ;

wherein R_2 and R_3 may be bonded together to form a C_{2-8} alkyl group;

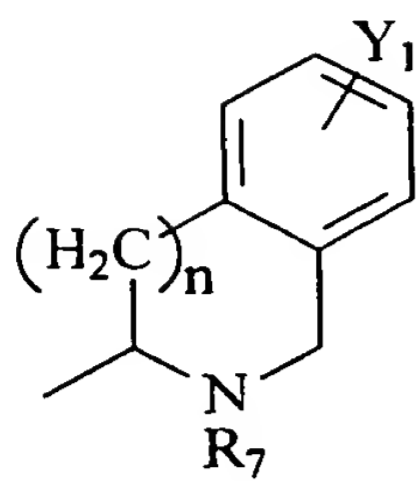
R_4 is hydrogen, C_{1-8} alkyl, CO_2C_{1-8} alkylaryl substituted by one or more groups Y_1 , CH_2 aryl substituted by one or more groups Y_1 , or CO_2C_{1-8} alkyl;

Z is N, O or S; when Z is O or S, there is no R_5

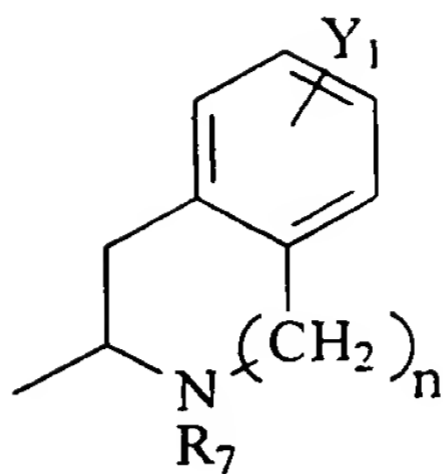
R_5 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $CH_2CO_2C_{1-8}$ alkyl, CO_2C_{1-8} alkyl or CH_2 aryl substituted by one or more groups Y_1 ;

n is 0, 1, 2 or 3;

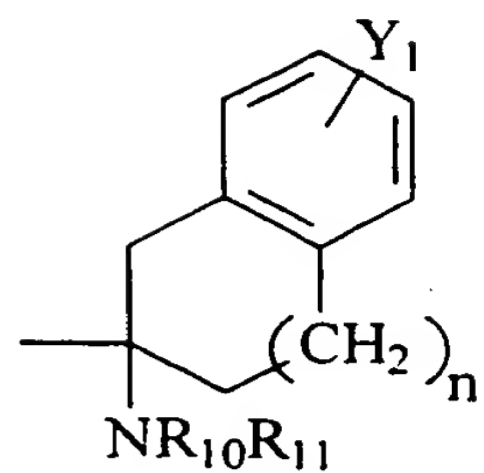
R_6 is a group selected from the group consisting of structures (a)-(bbb):



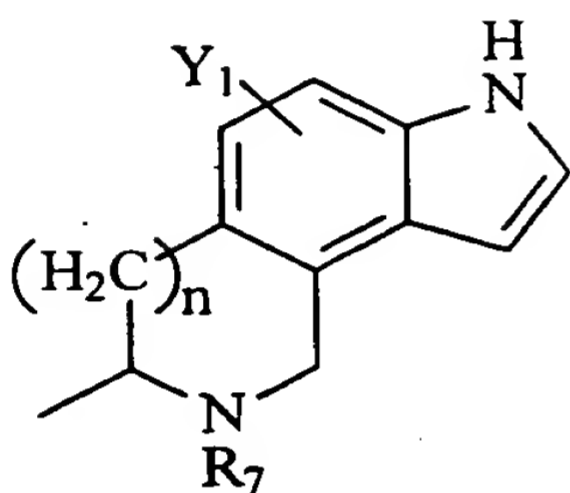
(a)



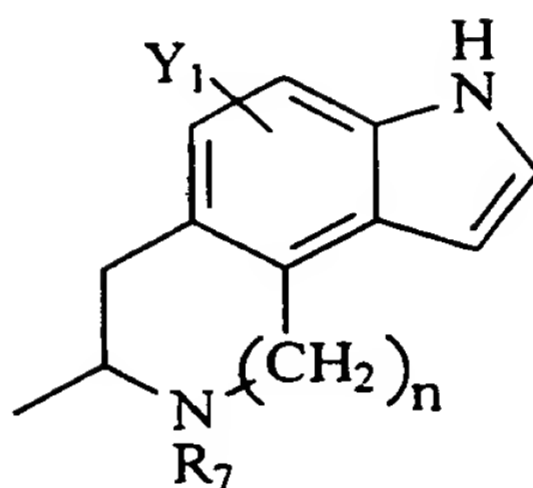
(b)



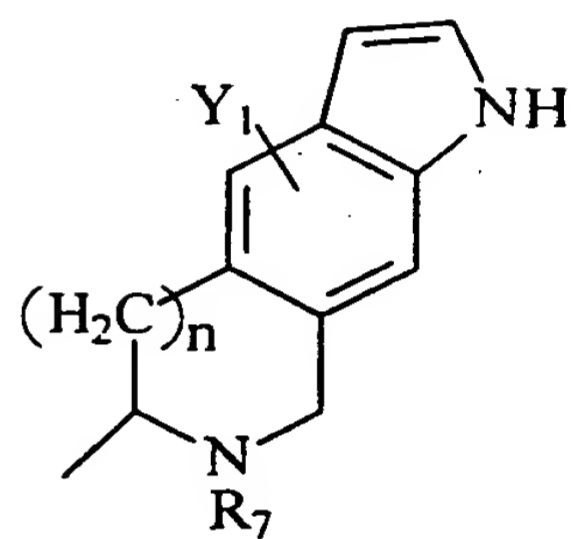
(c)



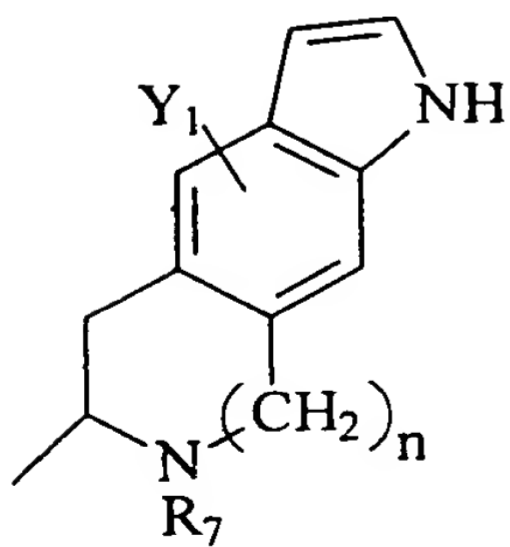
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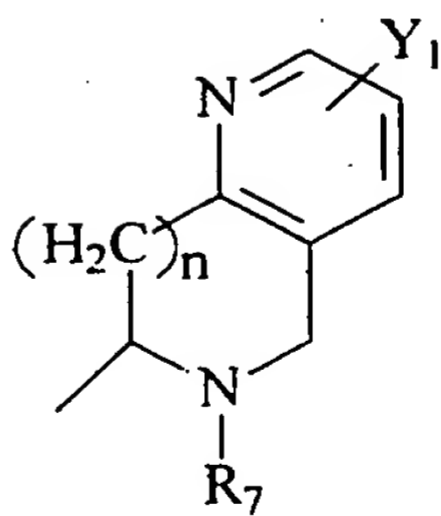
(e)



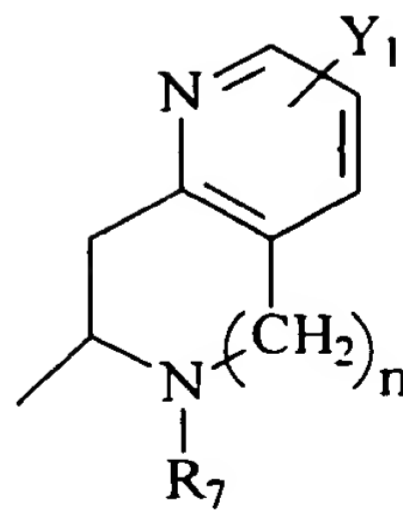
(f)



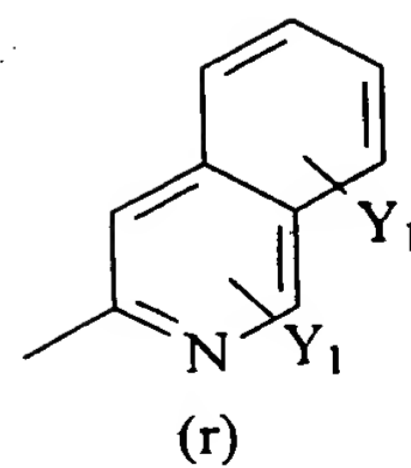
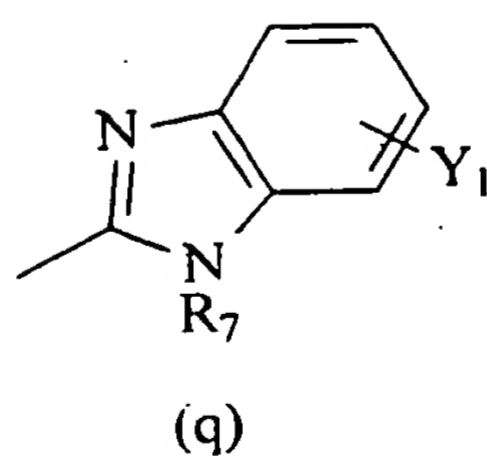
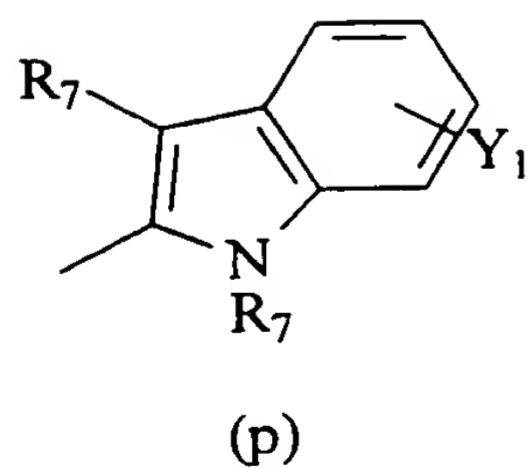
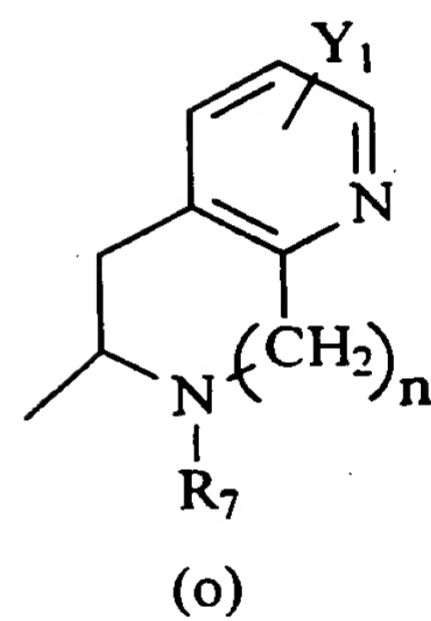
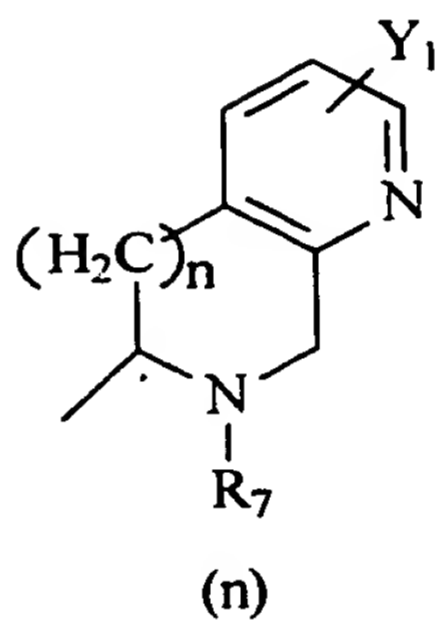
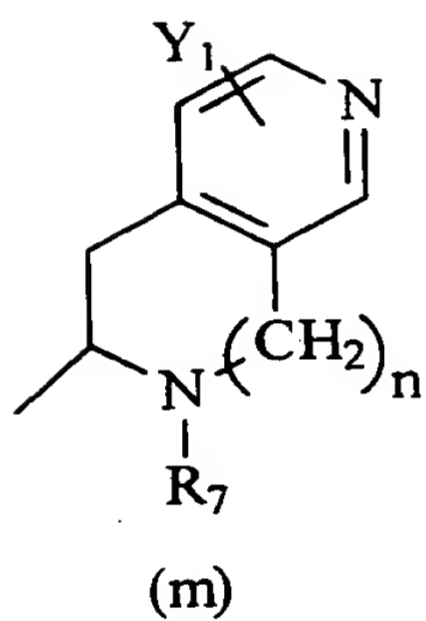
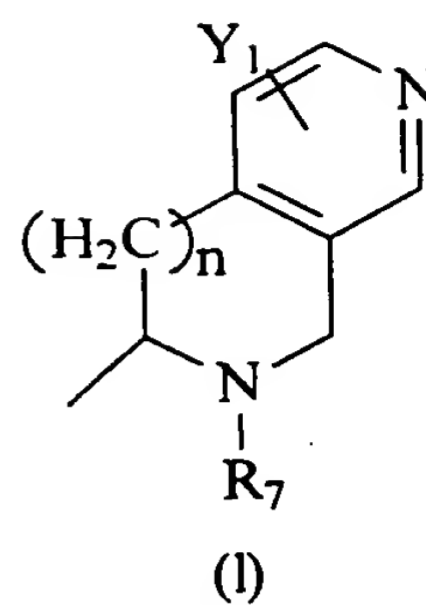
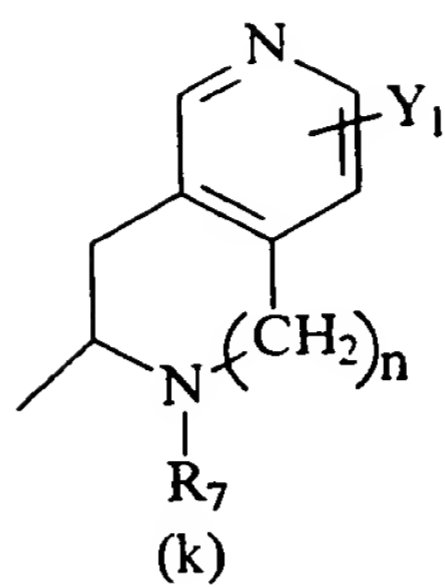
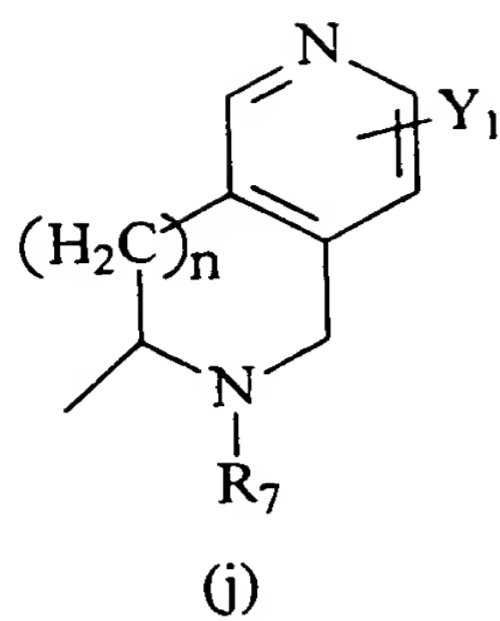
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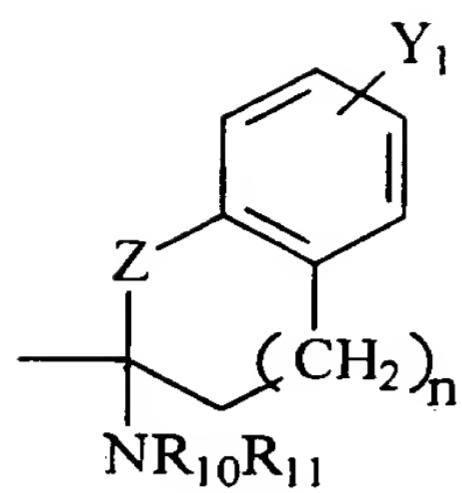
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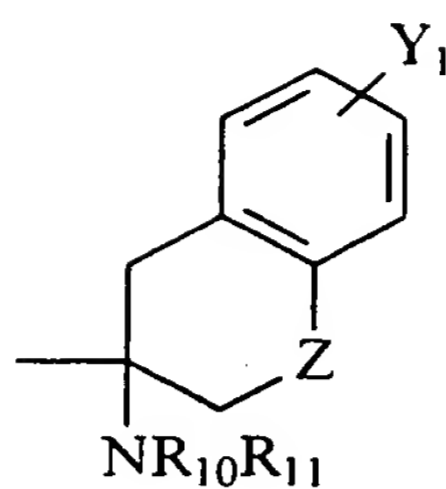
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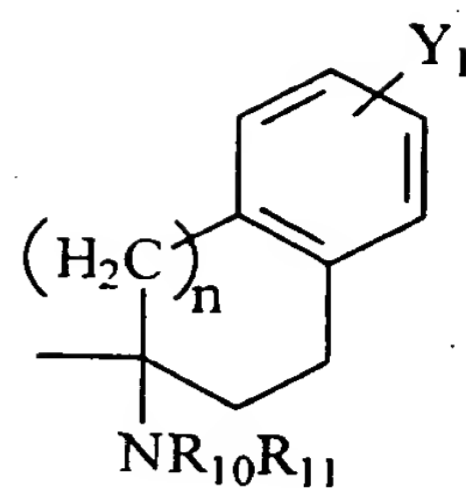
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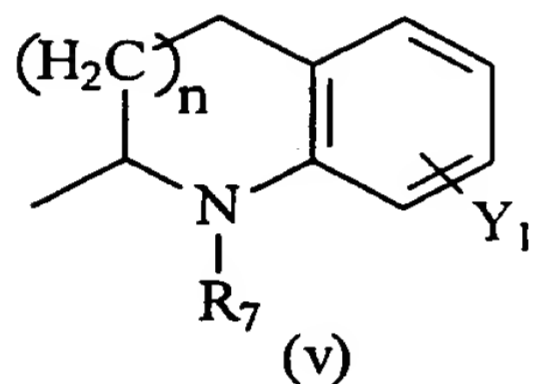
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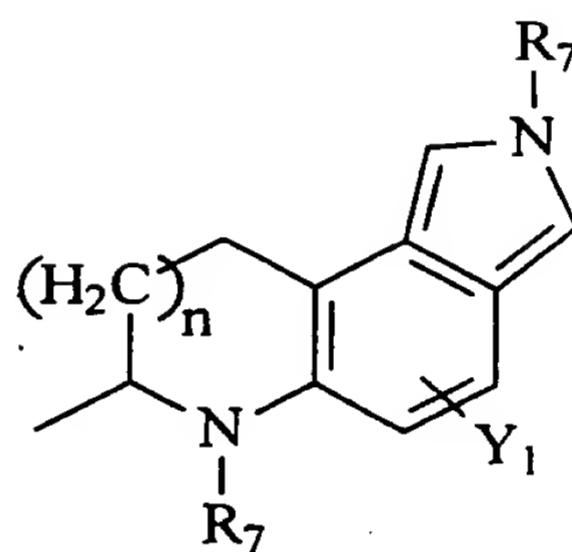
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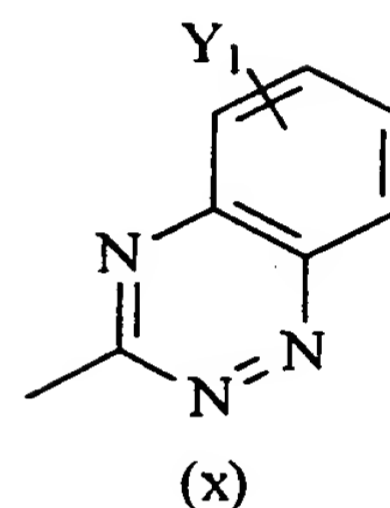
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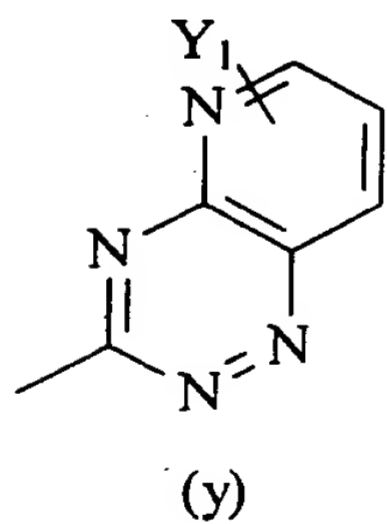
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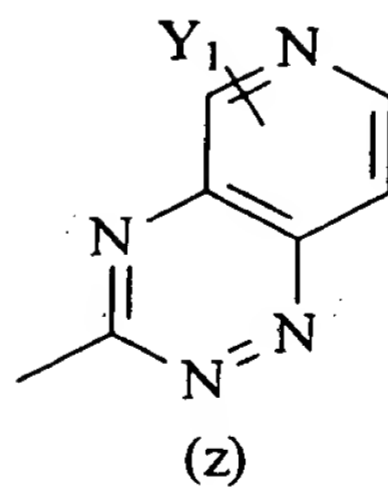
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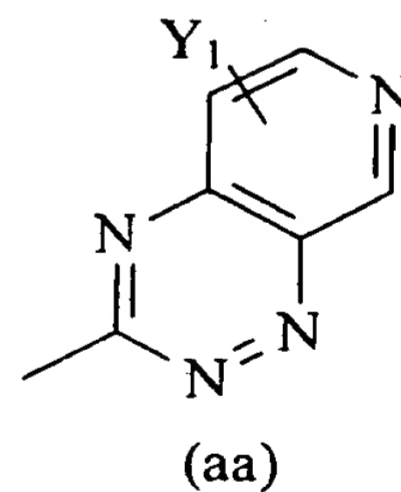
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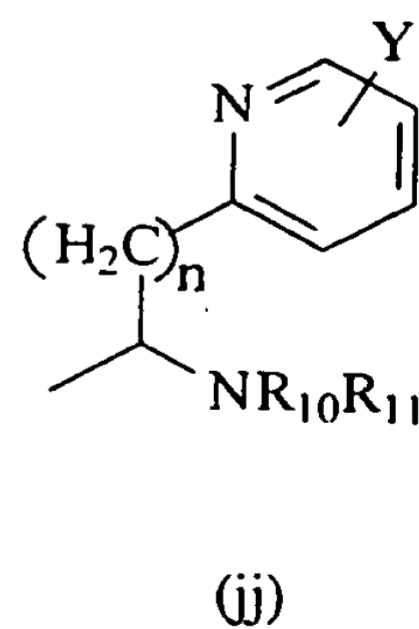
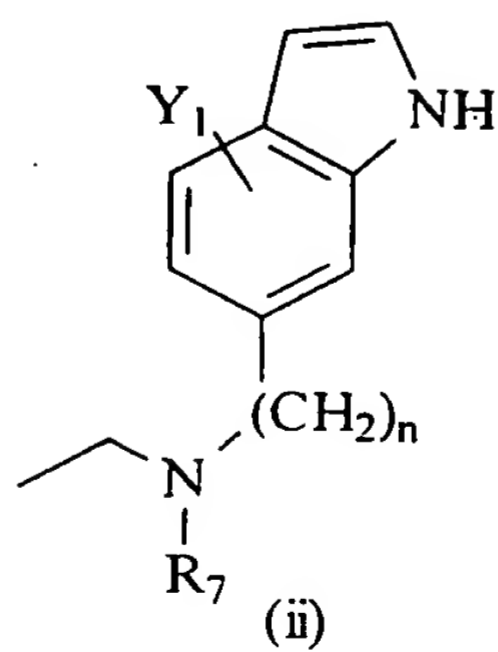
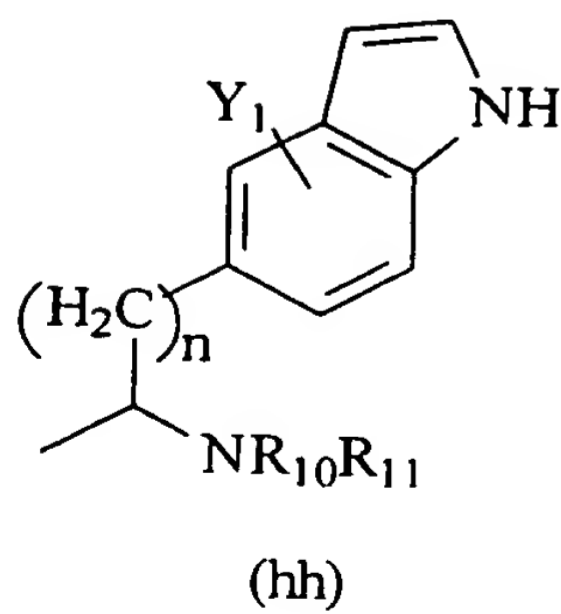
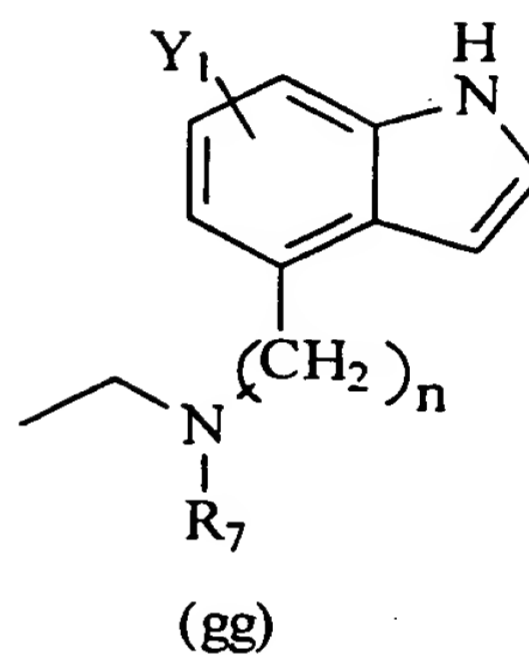
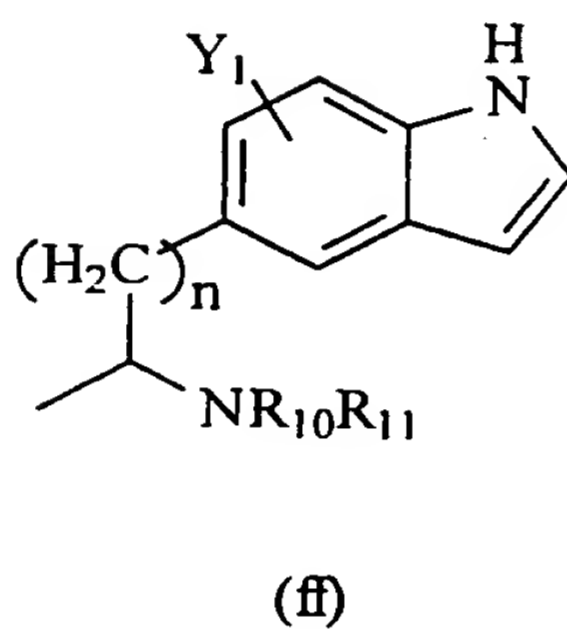
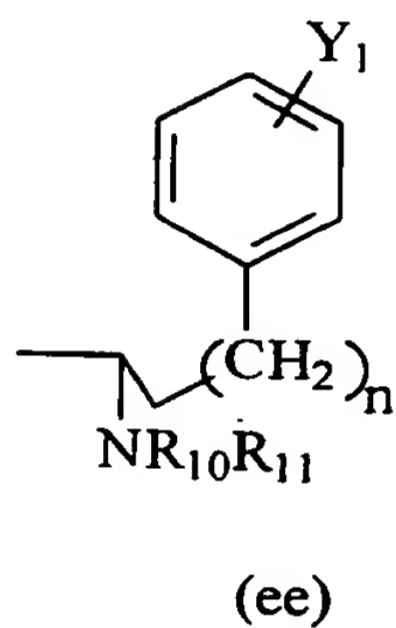
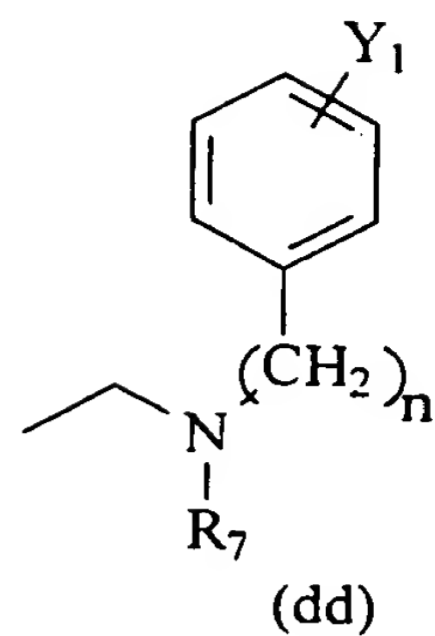
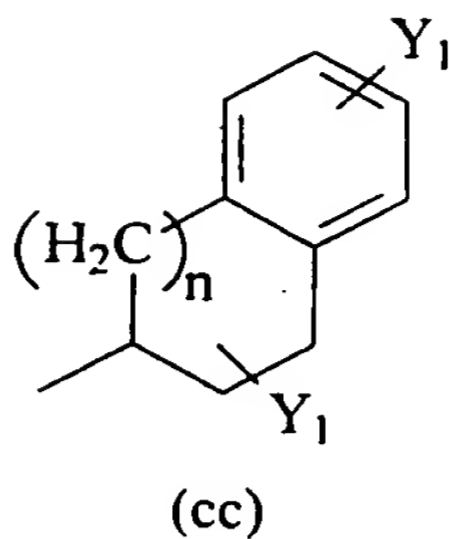
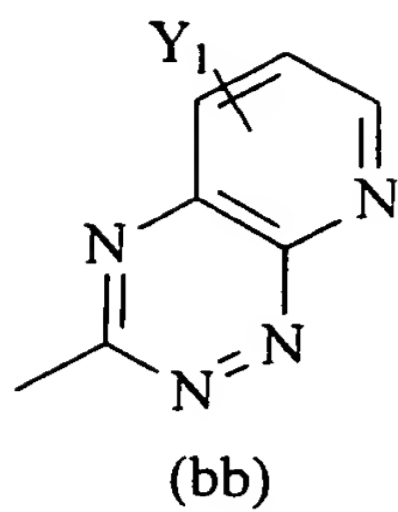
(y)



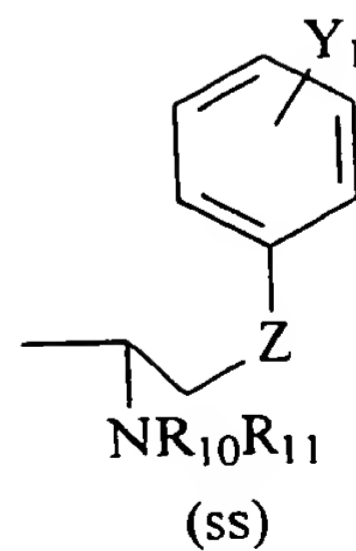
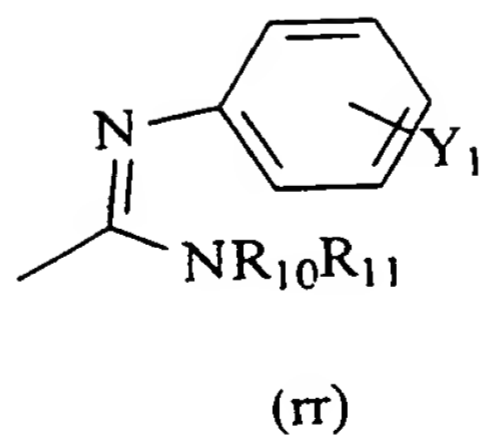
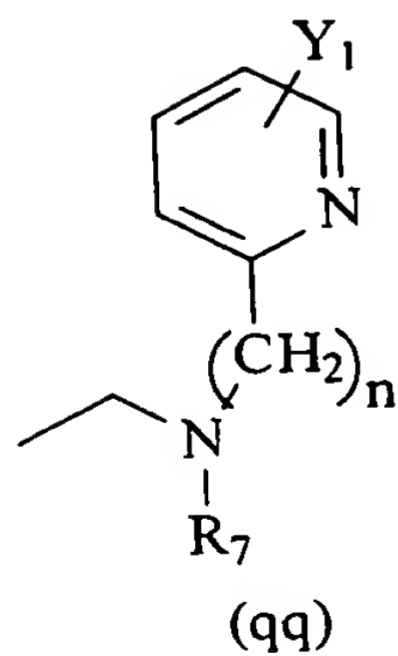
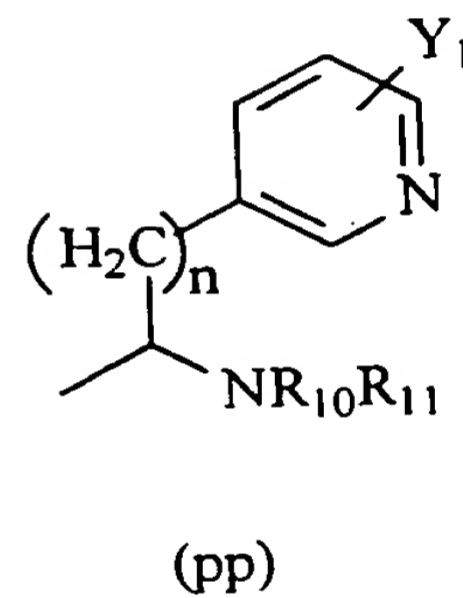
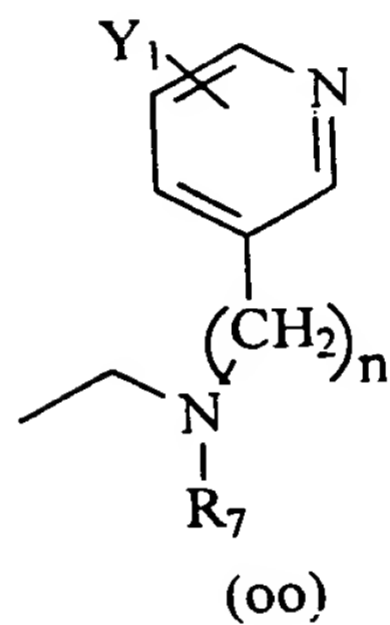
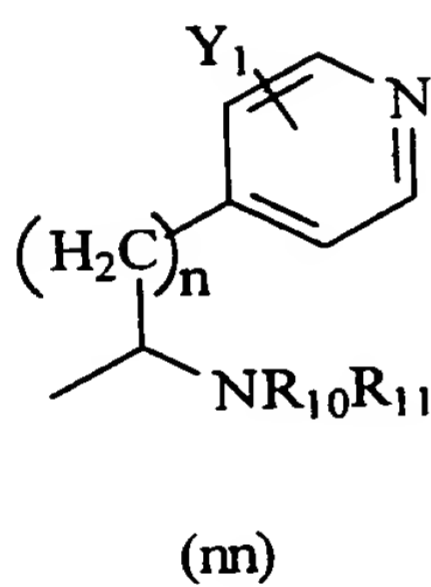
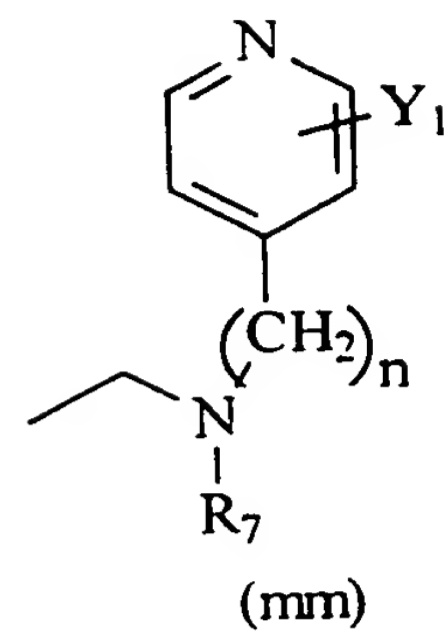
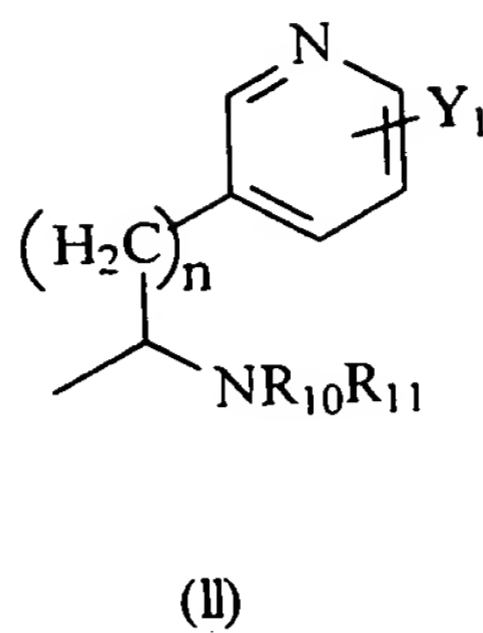
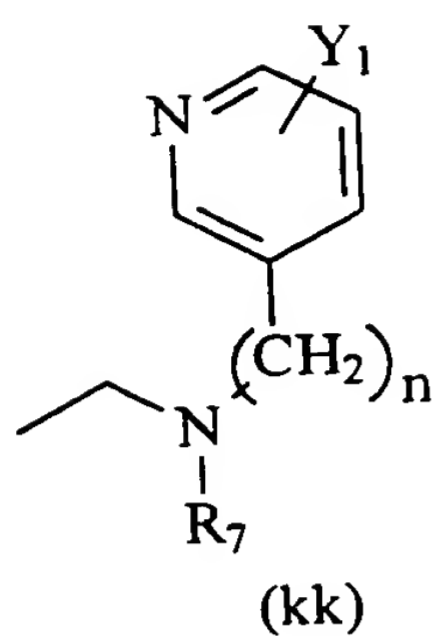
(z)



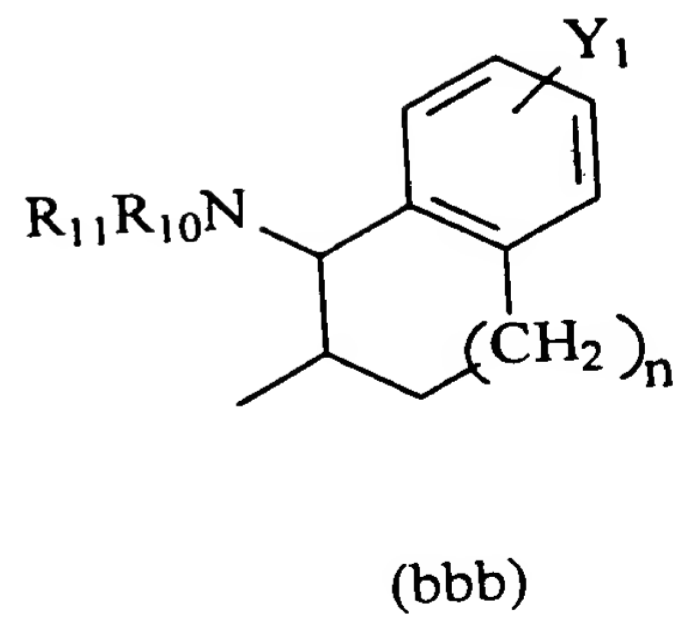
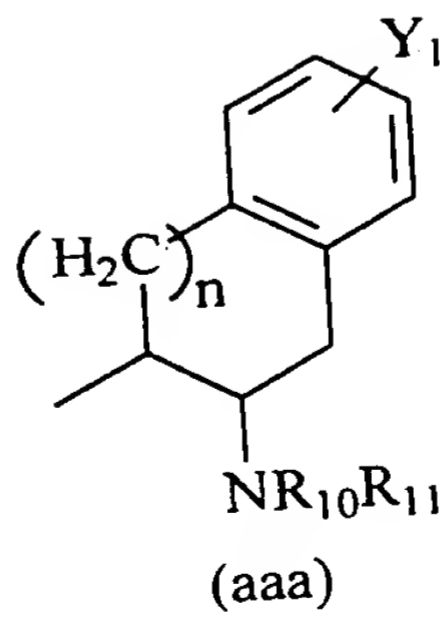
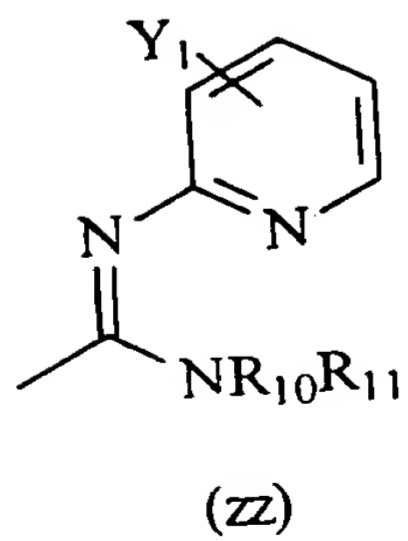
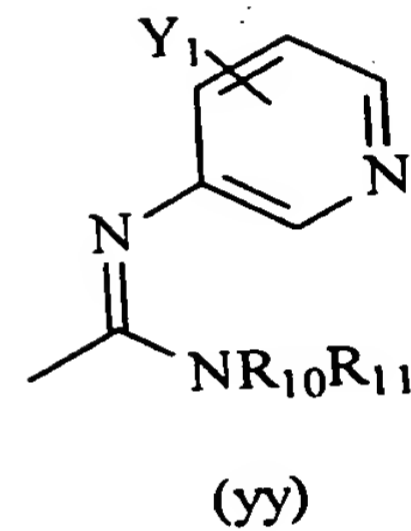
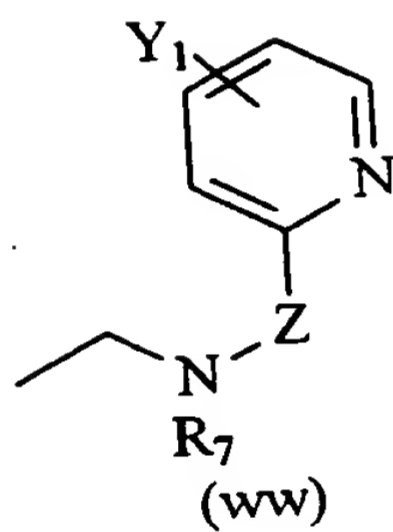
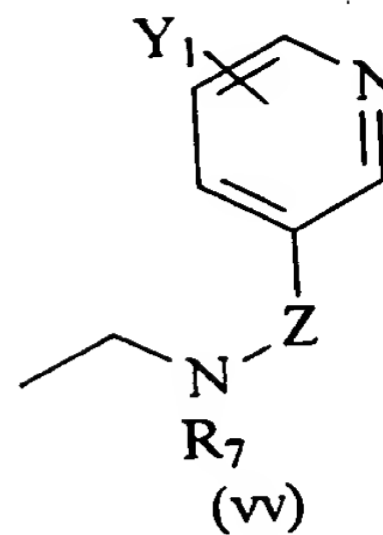
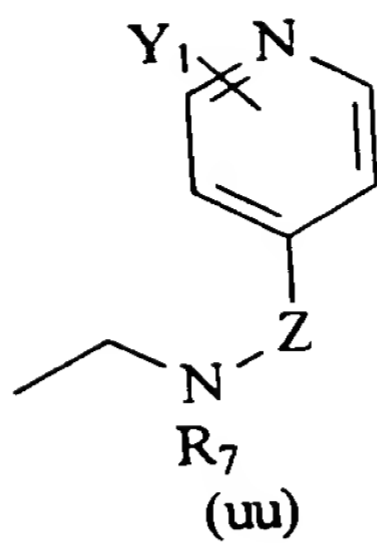
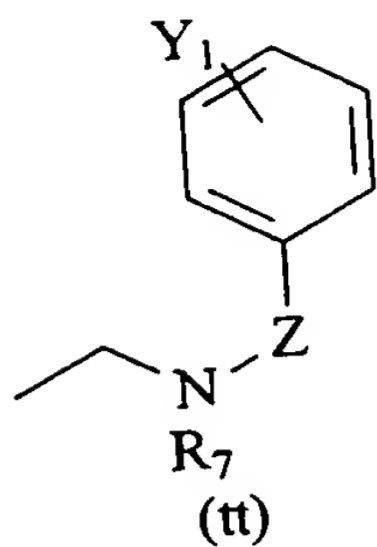
(aa)



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X_1 is hydrogen, C_{1-8} alkyl, C_{3-8} alkenyl, or C_{3-8} alkynyl;

X_2 is hydrogen, C_{1-8} alkyl, C_{3-8} alkenyl, or C_{3-8} alkynyl;

or X_1 and X_2 together form $=O$, $=S$, $=NH$;

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, $CH_2(CH_2)_nY_2$, or $C(=NH)NR_{16}R_{17}$;

R_8 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

R_9 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{10} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{11} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{12} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{13} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{14} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{15} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

R_{16} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$; and

R_{17} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or
 $CH_2(CH_2)_n Y_2$

or a pharmaceutically acceptable salt thereof.

14. (Currently Amended) The pharmaceutical composition of claim 13, wherein said
 kappa opioid receptor antagonist is a compound of formula (I), wherein R_1 , R_4 , R_5 , Y_1 , Y_2 , Z ,
 n , X_1 , X_2 , and R_7 - R_{17} are as ~~indicated above~~ in Claim 13;

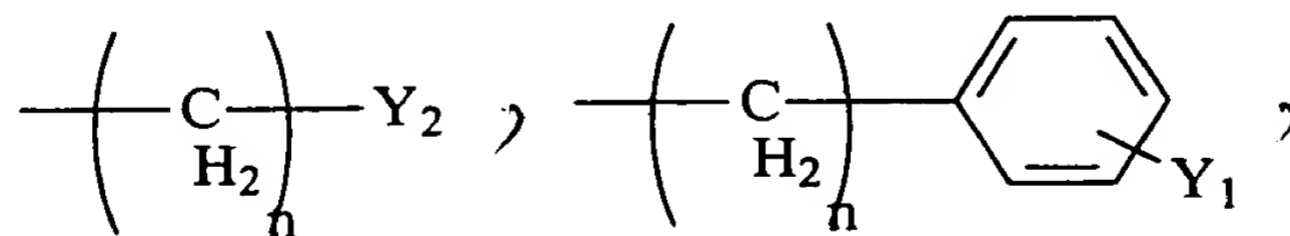
Y_3 is H;

R_2 and R_3 are each, independently, H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, or CH_2 aryl
 substituted by one or more substituents Y_1 ; and

R_6 is a group having a formula selected from the group consisting of structures (a)-
 (cc).

15. (Currently Amended) The pharmaceutical composition of claim 13, wherein said
 kappa opioid receptor antagonist is a compound of formula (I), wherein Y_1 , Y_2 , R_4 , R_5 , Z , n ,
 X_1 , X_2 and R_8 - R_{15} are as ~~indicated above~~ in Claim 13;

R_1 is C_{1-8} alkyl, or one of the following structures:



Y_3 is H;

R_2 and R_3 are each, independently, H or C_{1-8} alkyl, wherein R_2 and R_3 cannot both be H at the same time;

R_6 is a formula selected from the structures (a)-(r) ~~shown above~~; and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

16. (Currently Amended) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y_1 , Z, n, X_1 , X_2 and R_8 - R_{15} are as ~~noted above~~ in Claim 13;

R_1 is C_{1-8} alkyl;

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each, independently, H or methyl, wherein R_2 and R_3 cannot both be H at the same time;

R_4 is H, C_{1-8} alkyl, CO_2C_{1-8} alkyl, ~~aryl~~ or CH_2 aryl substituted by one or more substituents Y_1 and the stereocenter adjacent to R_4 is in an (S) configuration;

R_5 is H, C_{1-8} alkyl, $CH_2CO_2C_{1-8}$ alkyl;

R_6 is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

17. (Currently Amended) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y_1 , Z , n , X_1 , X_2 and R_8 - R_{14} are as indicated above in Claim 13;

R_1 is methyl,

Y_2 is H , CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H ;

R_2 and R_3 are each H or methyl, such that when R_2 is H , R_3 is methyl and vice versa;

R_4 is C_{1-8} alkyl, or CO_2C_{1-8} alkyl, and the stereocenter adjacent to R_4 has a configuration of (S);

R_5 is H ;

R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

R_7 is H , C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 or $CH_2(CH_2)_nY_2$.

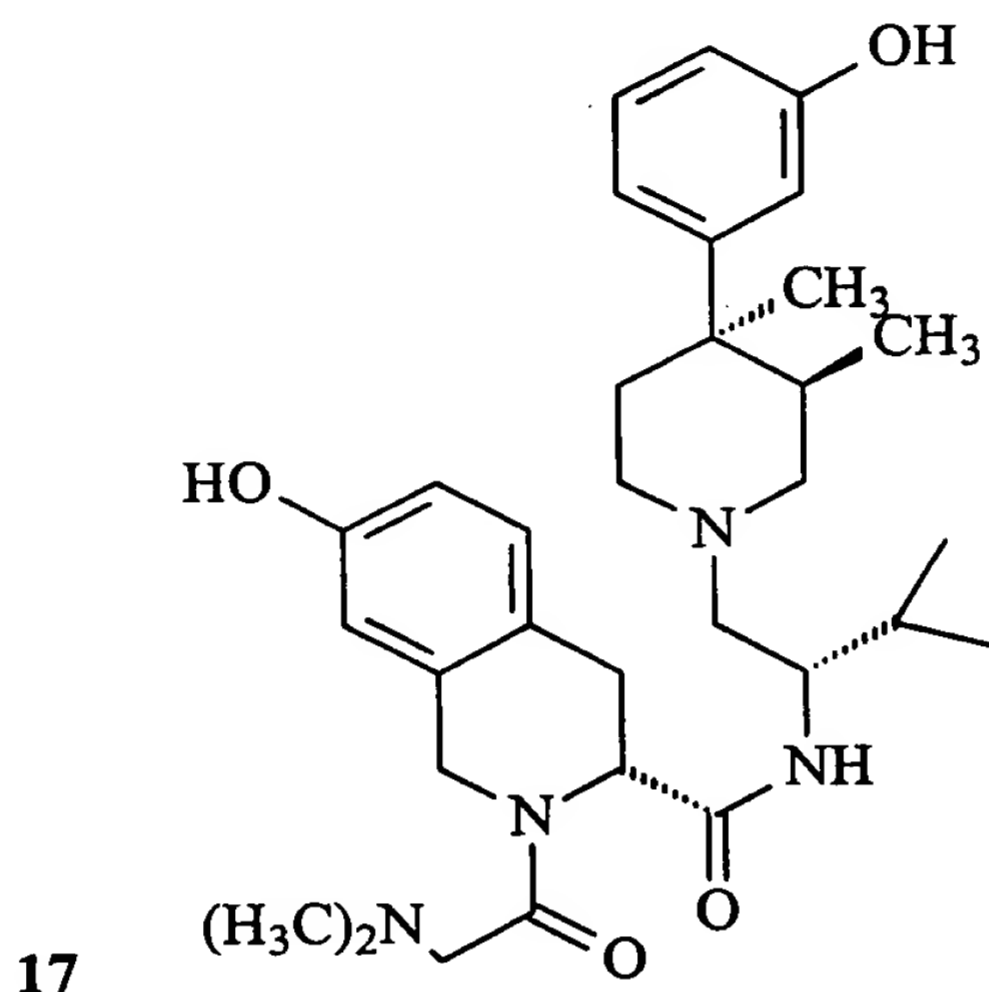
18. (Original) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound selected from formulae 14-21 of Fig. 1.

19. (Original) The pharmaceutical composition of claim 13, wherein said composition is an injectable composition.

20. (Original) The pharmaceutical composition of claim 13, wherein said composition is an orally administrable composition.

21. (Original) The pharmaceutical composition of claim 20, wherein said orally administrable composition is in a form selected from the group consisting of tablets, capsules, troches, powders, solutions, dispersions, emulsions and suspensions.

22. (Currently Amended) The kappa ~~opioid~~ opioid receptor antagonist according to Claim 7, having the chemical formula:



23. (New) The method of binding a kappa opioid receptor in a subject in need thereof, as claimed in claim 1, wherein R_1 is C_{1-8} alkyl; $(CH_2)_n-Y_2$; $(CH_2)_n$ -phenyl- Y_1 ; or $(CH_2)_n$ -pyridyl- Y_1 , and R_6 is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb), and wherein Q, Y_1 - Y_3 , R_2 - R_5 , Z, n, X_1 , X_2 , and R_7 - R_{17} are as in Claim 1.

24. (New) The kappa opioid receptor antagonist compound as claimed in claim 7, wherein R_1 is C_{1-8} alkyl; $(CH_2)_n-Y_2$; $(CH_2)_n$ -phenyl- Y_1 ; or $(CH_2)_n$ -pyridyl- Y_1 , and R_6 is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb), and wherein Q, Y_1 - Y_3 , R_2 - R_5 , Z, n, X_1 , X_2 , and R_7 - R_{17} are as in Claim 7.

25. (New) The pharmaceutical composition as claimed in claim 13, wherein R_1 is C_{1-8} alkyl; $(CH_2)_n-Y_2$; $(CH_2)_n$ -phenyl- Y_1 ; or $(CH_2)_n$ -pyridyl- Y_1 , and R_6 is a group selected from

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the group consisting of structures (a)-(w) and (cc)-(bbb), and wherein Q, Y₁-Y₃, R₂-R₅, Z, n, X₁, X₂, and R₇-R₁₇ are as in Claim 13.--
